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Declared competing interests of authors: Mike Thomas is a member of the Health Technology Assessment (HTA) Primary Care, Community and Preventive Interventions (PCCPI) Panel. In the last 3 years he has received speaker's honoraria for speaking at sponsored meetings or satellite symposia at conferences from the following companies, marketing respiratory and allergy products: Aerocrine, GlaxoSmithKline (GSK) and Novartis International AG. He has received honoraria for attending advisory panels with Aerocrine, AstraZeneca, Boehringer Ingelheim, GSK and Novartis. He has received sponsorship to attend international scientific meetings from GSK and AstraZeneca and has received funding for research projects from GSK. He is a member of the British Thoracic Society (BTS)/Scottish Intercollegiate Guidelines Network (SIGN) Asthma Guideline Group and the National Institute for Health and Care Excellence (NICE) Asthma Guideline Group. Paul Little is Editor-in-Chief of the *Programme Grants for Applied Research* journal and is a member of the National Institute for Health Research (NIHR) Journals

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Abstract

A randomised controlled study of the effectiveness of breathing retraining exercises taught by a physiotherapist either by instructional DVD or in face-to-face sessions in the management of asthma in adults

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Background: Asthma control is suboptimal, resulting in quality of life (QoL) impairment and costs. Breathing retraining exercises have evidence of effectiveness as adjuvant treatment, but are infrequently used.

Objectives: To transfer the contents of a brief (three-session) physiotherapist-delivered breathing retraining programme to a digital versatile disc (DVD) and booklet format; to compare the effectiveness of the self-guided intervention with that of 'face-to-face' physiotherapy and usual care for QoL and other asthma-related outcomes; to perform a health economic assessment of both interventions; and to perform a process evaluation using quantitative and qualitative methods.

Design: Parallel-group three-arm randomised controlled trial.

Setting: General practice surgeries in the UK.

Participants: In total, 655 adults currently receiving asthma treatment with impaired asthma-related QoL were randomly allocated to the DVD ($n = 261$), physiotherapist ($n = 132$) and control (usual care) ($n = 262$) arms in a 2 : 1 : 2 ratio. It was not possible to blind participants but data collection and analysis were performed blinded.

Interventions: Physiotherapy-based breathing retraining delivered through three 'face-to-face' respiratory physiotherapist sessions or a self-guided programme (DVD plus our theory-based behaviour change booklet) developed by the research team, with a control of usual care.

Main outcome measures: The primary outcome measure was asthma-specific QoL, measured using the Asthma Quality of Life Questionnaire (AQLQ). Secondary outcomes included asthma symptom control [Asthma Control Questionnaire (ACQ)], psychological state [Hospital Anxiety and Depression Scale (HADS)], hyperventilation symptoms (Nijmegen questionnaire), generic QoL [EuroQol-5 Dimensions (EQ-5D)], assessments of airway physiology (spirometry) and inflammation (exhaled nitric oxide) and health resource use and costs. Assessments were carried out at baseline and at 3, 6 and 12 months post randomisation. Patient engagement and experience were also assessed using quantitative and qualitative methods.

Results: Primary efficacy analysis was between-group comparison of changes in AQLQ scores from baseline to 12 months in the intention-to-treat population with adjustments for prespecified covariates. Significant improvements occurred in the DVD group compared with the control group [adjusted mean difference 0.28, 95% confidence interval (CI) 0.11 to 0.44; $p < 0.001$] and in the face-to-face physiotherapy group compared with the control group (adjusted mean difference 0.24, 95% CI 0.04 to 0.44; $p < 0.05$), with equivalence between the DVD and the face-to-face physiotherapy groups (adjusted mean difference 0.04, 95% CI –0.16 to 0.24). In all sensitivity analyses, both interventions remained significantly superior to the control and equivalence between the interventions was maintained. In other questionnaire outcome measures and in the physiological measures assessed, there were no significant between-group differences. Process evaluations showed that participants engaged well with both of the active interventions, but that some participants in the DVD arm would have liked to receive tuition from a professional. Asthma health-care costs were lower in both intervention arms than in the control group, indicating 'dominance' for both of the interventions compared with the control, with lowest costs in the DVD arm. The rate of adverse events was lower in the DVD and face-to-face physiotherapy groups than in the control group.

Conclusions: Only 10% of the potentially eligible population responded to the study invitation. However, breathing retraining exercises improved QoL and reduced health-care costs in adults with asthma whose condition remains uncontrolled despite standard pharmacological therapy, were engaged with well by patients and can be delivered effectively as a self-guided intervention. The intervention should now be transferred to an internet-based platform and implementation studies performed. Interventions for younger patients should be developed and trialled.

Trial registration: Current Controlled Trials ISRCTN88318003.

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List of abbreviations

A&E	accident and emergency
ACQ	Asthma Control Questionnaire
ANCOVA	analysis of covariance
AQLQ	Asthma Quality of Life Questionnaire
BREATHE	Breathing REtraining for Asthma – Trial of Home Exercises
BTS	British Thoracic Society
CI	confidence interval
CONSORT	Consolidated Standards of Reporting Trials
COPD	chronic obstructive pulmonary disease
CRN	Clinical Research Network
DMEC	Data Monitoring and Ethics Committee
EQ-5D	EuroQol-5 Dimensions
FeNO	fraction of exhaled nitric oxide
FEV_1	forced expiratory volume in 1 second
FVC	forced volume vital capacity
GINA	Global Initiative for Asthma
GP	general practitioner
HADS	Hospital Anxiety and Depression Scale
HTA	Health Technology Assessment
ICER	incremental cost-effectiveness ratio
IPQ	Illness Perceptions Questionnaire
IQR	interquartile range
IRR	incidence rate ratio
ITT	intention to treat
KMO	Kaiser–Meyer–Olkin
LABA	long-acting beta-agonist
LOCF	last observation carried forward
LTRA	leukotriene receptor antagonist
MCID	minimal clinically important difference
MRC	Medical Research Council
NIHR	National Institute for Health Research
NNT	number needed to treat
PCRN	Primary Care Research Network
PEFR	peak expiratory flow rate
PETS	Problematic Experiences of Therapy Scale
PI	principal investigator
PP	per protocol
PPI	patient and public involvement
QALY	quality-adjusted life-year
QoL	quality of life
RCT	randomised controlled trial
SAP	statistical analysis plan
SCTU	Southampton Clinical Trials Unit
SD	standard deviation
SIGN	Scottish Intercollegiate Guidelines Network
TMG	Trial Management Group
TSC	Trial Steering Committee
WHO	World Health Organization

Plain English summary

Most adults with asthma have symptoms that affect their lives, despite taking appropriate medications, and many are interested in non-drug approaches. We compared breathing retraining delivered through 'face-to-face' physiotherapy sessions with both a self-guided programme [digital versatile disc (DVD) plus booklet] of breathing retraining that could be carried out at home and usual care. Adults with incompletely controlled asthma in primary care were randomised into one of these groups. They were assessed before starting the intervention and at 3, 6 and 12 months afterwards for asthma quality of life (QoL) and were also assessed with other questionnaire and physiological measures; in addition, qualitative interviews were carried out to obtain the perspectives of patients and an economic evaluation was performed.

We recruited 655 volunteers from general practice surgeries. QoL significantly improved in both active groups compared with usual care, with equivalent improvements between active groups. Patients reported feeling that the exercises were helpful and acceptable, although some participants who received the DVD would have appreciated talking to a physiotherapist. Lung function and inflammation were unaffected. There were consistent improvement trends in the active arms for symptom scores, rescue medication use, anxiety and depression and asthma attacks, but these improvements were not statistically significant and so could have occurred through chance. Asthma-related costs were lower in both of the active groups.

People with asthma felt and functioned better following breathing retraining delivered by either a DVD or a physiotherapist and programme costs were exceeded by savings from better asthma control, with the DVD being most cost-effective. Patients still had asthma but coped with it better. These simple exercises can be carried out at home and have the potential to improve asthma control and save money.

Scientific summary

Background

Asthma affects > 5 million people in the UK, with costs in excess of £1B annually. Although pharmacotherapy is effective and can provide full control for some, surveys repeatedly show that outcomes remain suboptimal, with persisting symptoms and quality of life (QoL) impairment for the majority. Symptoms attributed to dysfunctional breathing overlap with those of asthma and have been reported to be more frequent in people with asthma, providing a rationale for using breathing retraining to improve asthma control. Randomised controlled trials (RCTs) have reported beneficial outcomes from breathing retraining in asthma, particularly from physiotherapist-administered breathing exercises, which are now advocated in guidelines as adjuvant treatment for those who remain uncontrolled on pharmacological treatment. Previous research from members of this study group provided evidence supporting this recommendation, with two positive RCTs supporting physiotherapist-delivered breathing retraining. However, the cost-effectiveness of this intervention was not addressed and resource constraints mean that the majority of people with asthma who could benefit are not able to access a suitably trained respiratory physiotherapist. Two preliminary studies have investigated the use of breathing retraining delivered by videotape or digital versatile disc (DVD), with some evidence of effectiveness. Such self-guided programmes have the potential to be accessed easily, conveniently and inexpensively by large numbers of people. No studies have compared the clinical effectiveness and cost-effectiveness of a self-guided programme with those of face-to-face breathing retraining interventions.

We hypothesised that breathing retraining exercises taught as a self-guided programme would improve asthma-related QoL above 'usual care' and would be equivalent to 'face-to-face' physiotherapist instruction.

Objectives

- To use an iterative patient-focused approach to transfer the contents of a three-session physiotherapist-delivered breathing retraining programme, previously shown to improve asthma control, to a self-guided format that is acceptable to patients.
- To perform a RCT in adults with impaired asthma control, comparing the effectiveness of breathing retraining delivered by the self-guided programme with the effectiveness of a face-to-face breathing retraining programme delivered by a respiratory physiotherapist and with usual care, for asthma-related QoL and other asthma control measures.
- To perform quantitative and qualitative process evaluations.
- To perform a health economic assessment using data collected from the trial and from general practice clinical records.

Methods

Trial design

We carried out a pragmatic, observer-blinded, three-arm, parallel-group RCT comparing a breathing retraining programme delivered in DVD format with a breathing retraining programme delivered face-to-face by a physiotherapist and with a control of usual care for adults with asthma and impaired health status.

Participants

In total, 655 adult patients with diagnosed and currently treated asthma were recruited from 34 primary UK NHS general practices in the Wessex region.

Inclusion criteria

- Full practice registration for 12 months prior to enrolment.
- Age 16–70 years.
- Physician-diagnosed asthma in medical records.
- One or more anti-asthma medication prescriptions in the previous year.
- Impaired asthma-related health status [Asthma Quality of Life Questionnaire (AQLQ) score of < 5.5].
- Able to give informed consent.

Exclusion criteria

- Asthma dangerously unstable and in need of urgent medical review at baseline.
- Concomitant chronic obstructive pulmonary disease if forced expiratory volume in 1 second (FEV_1) is < 60% predicted.

Broad entry criteria were pragmatically used (with the inclusion of smokers and not insisting on physiological demonstration of reversible airflow obstruction) to allow the generalisability of the research findings to mild-to-moderate UK asthma populations treated in primary care NHS practice.

Outcome measures

Primary outcome

The primary outcome was the between-group [intention-to-treat (ITT)] 12-month asthma-specific health status (AQLQ score), adjusted for prespecified covariates.

Secondary outcomes

- Prespecified sensitivity analyses on the main outcome [unadjusted analysis of between-group ITT AQLQ score changes, per-protocol (PP) between-group AQLQ score changes, sensitivity analysis including patients without full AQLQ data].
- Analysis of the between-group ITT and PP changes in:
    - Asthma Control Questionnaire (ACQ) scores
    - lung function [FEV_1, FEV_1-to-forced volume vital capacity (FVC) ratio, peak expiratory flow rate (PEFR)]
    - fraction of exhaled nitric oxide (FeNO)
    - generic health status [EuroQol-5 Dimensions (EQ-5D)]
    - anxiety and depression scores [Hospital Anxiety and Depression Scale (HADS)]
    - hyperventilation (Nijmegen) questionnaire scores
    - asthma exacerbations (oral corticosteroid courses)
    - bronchodilator use
    - asthma-related health resource use
    - cost-effectiveness/utility
    - patient-reported process evaluations (qualitative assessments and questionnaires)
    - patient engagement in breathing retraining programmes.

Study procedures

Development phase

We transferred an existing 'face-to-face' programme of breathing retraining taught by physiotherapists to patients with dysfunctional breathing to a self-guided programme format delivered through a DVD with printed supportive materials, and undertook qualitative piloting of these materials to optimise acceptability and effectiveness. Patient educational materials were developed by a team including physicians, physiotherapists,

health psychologists, communications technology specialists and patient representatives. The DVD and accompanying booklet were created iteratively with extensive patient input. The DVD content included:

- detailed explanations and illustrations of how to carry out the exercises, with footage showing a physiotherapist teaching the exercises to patients
- motivational components explaining the rationale for the exercises and addressing common doubts and concerns.

The materials were piloted with a panel of 29 members of the target population, purposively sampled for diversity in terms of age, sex, education and symptom profile. In audio-recorded face-to-face and telephone interviews we used open-ended questions to explore attitudes to the proposed treatment method in the context of health beliefs and then used 'think-aloud' methods to elicit reactions to the proposed materials, with modification of the scripts based on this feedback. Professional production of the DVD and booklet were undertaken and the materials were reviewed by the panel, who provided final feedback in face-to-face and telephone interviews.

Randomised controlled trial

Potentially eligible patients were identified by computer searches of general practice clinical and prescribing records. These patients were mailed the study information and an invitation letter, and were asked to complete the AQLQ and return it by post. Those with an AQLQ score of < 5.5 were recruited. Patients were seen at their general practice by a research nurse for a baseline assessment, consenting and randomisation. The baseline assessment consisted of assessment of clinical data (smoking status, asthma history, comorbidities, medication use), questionnaire data [disease-specific health status (AQLQ), Nijmegen hyperventilation questionnaire, ACQ, generic health status (EQ-5D), anxiety and depression (HADS)] and physiological data [spirometry (FEV_1, FEV_1-to-FVC ratio, PEFR), measured with a standardised calibrated portable spirometer; FeNO, measured with a NIOX MINO® portable monitor (Circassia Ltd, Oxford, UK)]. Randomisation was achieved by the study nurse telephoning the Southampton Clinical Trials Unit (SCTU) telephone randomisation service. Follow-up appointments were also arranged.

All consenting participants received postal questionnaires at 3 and 6 months and a final assessment visit at 12 months post randomisation. Those randomised to usual care received no other additional attention. Those randomised to the DVD were also provided with the booklet. Those randomised to face-to-face physiotherapy received three sessions (30–40 minutes each) with a respiratory physiotherapist at their general practice, at 2-weekly intervals following randomisation, and also received the instructional booklet. The final 12-month assessment was performed by a different study nurse blinded to randomisation group. The assessment consisted of the same clinical, questionnaire and physiological measurements performed at baseline, plus a short questionnaire exploring participants' perceptions and experiences of being in the trial and adherence and collection of routine clinical data.

A group of participants in the active arms selected by purposive sampling underwent qualitative interviews to assess their experiences of the interventions, until data saturation was achieved.

Statistical methods

The primary statistical analysis consisted of a repeated-measures mixed model using the 12-month AQLQ score across the three arms with adjustments for prespecified covariates [baseline AQLQ score, general practice, age, sex, smoking status, British Thoracic Society (BTS) treatment step, baseline HADS score and baseline Nijmegen questionnaire score], with pairwise comparisons between the DVD group and the control group, the physiotherapy group and the control group (superiority study) and the DVD group and the physiotherapy group (equivalence study, equivalence margin 0.3).

Results

Recruitment, retention and missing data

The recruitment target of 585 was increased to 655 by the Data Monitoring and Ethics Committee as an early unblinded analysis suggested a slightly higher dropout rate in the DVD arm. We successfully randomised 655 patients from 34 primary care sites. A total of 15,203 invitation letters were mailed, with 1481 responses received (response rate 9.7%). In total, 680 (45.9%) respondents were ineligible and 655 (81.8% of eligible respondents) were randomised, 261 (39.8%) to the DVD group, 262 (40.0%) to the control (usual care) group and 132 (20.2%) to the physiotherapy group. All 655 randomised participants were included in the ITT population. The PP population included 556 participants (DVD, $n = 215$; physiotherapy, $n = 110$; control, $n = 231$; 84.9% of the randomised population). A very low proportion of data were missing for all other questionnaires (< 2%). Spirometry data (FEV_1, FEV_1-to-FVC ratio) were missing for 4% of participants and FeNO values were missing for 7.5% of participants; missing data values were similar between treatment arms. Only 21 patients withdrew (3.2%), with similar rates of withdrawal between arms. The AQLQ was returned at 12 months by 556 participants and at one or more follow-up points by all 655 participants.

Primary outcome

In the primary efficacy analysis, the between-group comparison of 12-month AQLQ scores in the ITT population adjusted for prespecified covariates, we observed a statistically significant improvement in mean AQLQ score in the DVD arm compared with the control arm [adjusted mean difference 0.28, 95% confidence interval (CI) 0.11 to 0.44] and in the physiotherapy arm compared with the control arm (adjusted mean difference 0.24, 95% CI 0.04 to 0.44), confirming the superiority of both active arms over usual care. The adjusted mean difference between the DVD arm and the physiotherapy arm was 0.04 (95% CI –0.16 to 0.24), confirming equivalence of the active arms. In subdomain analysis, the largest improvements in the active arms compared with usual care were in the emotions domain (DVD vs. control: adjusted mean difference 0.38, 95% CI 0.16 to 0.60; physiotherapy vs. control: adjusted mean difference 0.43, 95% CI 0.16 to 0.71); significant improvements were also seen for symptoms, activities and environment in the DVD arm compared with usual care and for symptoms for the physiotherapy arm compared with usual care, with no significant differences between the active arms. The statistically significant differences were largely unchanged in the sensitivity analyses, with minor changes in magnitude. Analysis of the 3-month and 6-month AQLQ changes showed improvements in both active arms compared with the control arm by the first assessment, which were maintained or increased over 12 months. In the DVD arm, the improvements in mean total AQLQ score from baseline in the ITT population were 0.9 at 3 months, 1.0 at 6 months and 1.1 at 12 months; in the physiotherapy arm the equivalent figures were 1.0, 1.1 and 1.1 respectively. In the control arm, improvements in mean total AQLQ score from baseline were 0.6, 0.6 and 0.8 respectively.

An analysis in the ITT population of individual patient data using a cut-off point of 0.5 to define a clinically important change showed that 62% of participants in the DVD group improved over 12 months, compared with 64% in the physiotherapy group and 56% in the control group. The figures for deterioration were 5%, 4% and 8% respectively. The proportions improving in the PP population were slightly higher. A number needed to treat (NNT) analysis showed a NNT of eight for the DVD group compared with usual care, seven for the physiotherapy arm compared with usual care and 41 for the physiotherapy arm compared with the DVD arm.

Secondary outcomes

Physiology

There were no significant changes in lung function within or between treatment arms. Median (interquartile range) FeNO changes between baseline and 12 months were minor [DVD: from 21 parts per billion (p.p.b.) (14–35 p.p.b.) to 20 p.p.b. (13–33 p.p.b.); physiotherapy: from 23 p.p.b. (15–33 p.p.b.) to 21 p.p.b. (13–32 p.p.b.); control: from 23 p.p.b. (14–34 p.p.b.) to 20 p.p.b. (13–34 p.p.b.)], with no statistically

significant between-group differences when adjusted for covariates. These data indicate that breathing retraining by either modality did not significantly affect airway physiology or inflammation and so did not affect the pathophysiology of asthma.

Questionnaires

We found no significant between-group changes in asthma symptom control (ACQ), anxiety scores or hyperventilation symptom scores in either the ITT population or the PP population, although there were modest within-group changes from baseline in all within-group analyses and consistent trends favouring the intervention groups above the control group. There was a small but statistically significant improvement in depression scores in the DVD group compared with the control group.

Asthma attacks

Only 12% of the ITT population had one or more asthma attack over the 12-month period. The proportion of patients in the three randomisation groups (DVD, physiotherapy, control) having one or more asthma attack was 9%, 11% and 15% respectively. There was no statistically significant difference in exacerbation rate between the DVD group and the physiotherapy group ($p = 0.6$) or between the physiotherapy group and the control group ($p = 0.4$). The DVD group showed a marginal statistically significant reduction in exacerbations compared with the control group ($p = 0.06$). In a negative binomial regression model, the adjusted risk ratio for DVD compared with the control was 0.68 (95% CI 0.39 to 1.20) and for physiotherapy compared with the control was 0.85 (95% CI 0.43 to 1.67).

Short-acting bronchodilator use

A between-group analysis of rescue medication use in the 12 months post randomisation showed trends for lower bronchodilator use in the DVD group compared with the control group [incidence rate ratio (IRR) 0.83, 95% CI 0.68 to 1.03] and in the physiotherapy group compared with the control group (IRR 0.81, 95% CI 0.63 to 1.04).

Patient engagement and experience

In total, 95% of participants attended at least one of the three face-to-face physiotherapy sessions and 93% attended all three. Patient experience of the different intervention components was favourable, with most devoting time to practising techniques, the main hindrance being finding time to practise. Engagement was also good in the DVD group, although with lower engagement scores and practice times than in the physiotherapy group. Qualitative analysis revealed that both interventions were valued, although some in the DVD arm would have liked to be able to receive instruction from a practitioner.

Adverse events

The adverse event profile was as expected in the recruited population, with fewer events in the active arms than in the control group. There was no indication of treatment-related adverse effects from either the DVD programme or the physiotherapy programme, with both appearing to be well tolerated.

Economic evaluation

Costs were lower in both active treatment arms than in the control group, with the increased intervention costs offset by reductions in total costs, indicating a dominant health economic strategy favouring the DVD intervention. The quality-adjusted life-year changes were in the same direction as the primary outcome but were smaller. The DVD programme dominated the physiotherapy programme, having equivalent outcomes at a lower cost.

Conclusions

Using a rigorous patient-focused iterative development process, we produced a self-guided version of a face-to-face physiotherapy-based breathing retraining programme to improve QoL in people with asthma and performed a pragmatic RCT in primary care asthma patients to test the clinical effectiveness and

cost-effectiveness and patient acceptability of the programme. We showed that the self-guided intervention is superior to usual care and equivalent to face-to-face physiotherapy in improving asthma-related QoL in this patient group, and constitutes a dominant economic strategy. However, lung function and airway inflammation were not significantly affected, with the intervention helping people to cope better and suffer less despite not modifying the underlying pathophysiology of asthma. The exacerbation risk was one-third lower in the DVD group than in the usual-care group, but the study was underpowered to provide statistical significance for this outcome.

In conclusion, this intervention is potentially of benefit to large numbers of asthma patients and may save the NHS money.

Recommendations for future research

Larger studies to investigate a possible effect of the intervention on exacerbations, implementation studies and extensions to paediatric populations are needed.

Trial registration

This trial is registered as ISRCTN88318003.

Funding

Funding for this study was primarily provided by the Health Technology Assessment programme of the National Institute for Health Research, with additional financial support received from Comprehensive Local Research Networks.

Chapter 1 Introduction

Asthma affects > 5 million people in the UK and costs the NHS in excess of £1B. Although pharmacotherapy is effective and can provide full control for some patients,[1] surveys repeatedly show that outcomes remain suboptimal. A recent European survey showed that fewer than half of adults with asthma achieved good symptom control[2] and that quality of life (QoL) is affected for most, with consequent costs to the community both directly from health service use and indirectly from lost productivity. Many patients have concerns about taking regular medication, particularly inhaled corticosteroids. Surveys of complementary and alternative medicines in asthma show high levels of use, with up to 79% of adults and 78% of children reporting trying different treatments, include breathing modification.[3] Breathing techniques are among the most commonly used complementary techniques, with up to 30% reporting having used them to control their symptoms.[4] The James Lind Alliance and the patient organisation Asthma UK have both identified breathing exercises for asthma as a priority area for research.[5] Asthma encompasses a variety of phenotypes and different therapeutic approaches may be effective in different patients.[6] Symptoms attributed to dysfunctional breathing have been reported to be more frequent in people with asthma than in the general population.[7,8] A number of controlled studies have investigated breathing modification techniques and have reported beneficial outcomes. Breathing control techniques investigated have included the Butekyo breathing method[9–13] and yogic breathing.[14–16] Recent studies have shown clinically important effectiveness of physiotherapist-administered breathing exercises for people with asthma in the UK.[17–19] The evidence base for the effectiveness of breathing therapies for treating asthma has been assessed in several reviews. A recent systematic review of the effectiveness of physiotherapist-taught breathing retraining was carried out as part of a review of physiotherapy interventions in the treatment of respiratory diseases in adults.[20] This was a collaborative multidisciplinary review undertaken by the British Thoracic Society (BTS) and the Association of Chartered Physiotherapists in Respiratory Care (ACPRC), the respiratory clinical interest group of the Chartered Society of Physiotherapy (CSP). Its purpose was to critically appraise the evidence for respiratory physiotherapy techniques in respiratory diseases and it used an explicit evidence-based methodology. This consisted of an initial literature search, conducted by the Centre for Research and Dissemination (CRD), York, UK. Papers and abstracts identified were appraised and graded by two trained assessors using Scottish Intercollegiate Guidelines Network (SIGN) methodology, with recourse to a third assessor in the event of disagreements. The review found that 'Breathing exercises, incorporating reducing respiratory rate and/or tidal volume and relaxation training, should be offered to patients to help control the symptoms of asthma and improve QoL (Grade A)'. In the latest iterations of both the BTS/SIGN UK national asthma guideline[21] and the World Health Organization (WHO)-endorsed Global Initiative for Asthma (GINA) guideline,[22] breathing exercises are endorsed as adjuvant treatment for people with inadequately controlled asthma despite standard pharmacological treatment. Previous research from members of this study group has provided evidence supporting this recommendation. A prior Cochrane review of breathing exercises for asthma was performed in 2004,[23] before several large studies informing the BTS review had reported. This review stated that, because of the diversity of breathing exercises and outcomes used, it was impossible at that time to draw conclusions from the available evidence. The review stated that trends for improvements were noted in a number of outcomes and that large-scale studies were warranted to clarify the effectiveness of breathing exercises in the management of asthma. Subsequently, Slader *et al.*[3] reported a double-blind randomised controlled trial (RCT) of breathing techniques in asthma and concluded that breathing techniques may be useful in patients with mild asthma who use a reliever inhaler frequently. This Australian study investigated the effects of two different breathing retraining programmes taught by physiotherapists and delivered as videotaped instruction programmes that the participants completed at home, without face-to-face supervision. Both programmes were associated with improved health status and major reductions in bronchodilator use compared with baseline values.

These instructional interventions have subsequently been made available as internet downloads and have been used in Australia to improve asthma control in routine clinical practice. This study provided provisional evidence that breathing retraining programmes delivered in a self-guided audio-visual format are feasible and may potentially produce beneficial outcomes in asthma. A 2007 UK primary care-based

RCT[18] demonstrated that breathing retraining taught by a physiotherapist in face-to-face sessions significantly reduced respiratory symptoms and improved health-related QoL compared with usual care. The population studied consisted of community-treated asthmatics with mild and moderate disease. The contents of the breathing retraining programme in this study were very similar to those in our study, but only face-to-face instruction was investigated and no economic analysis was carried out. A Canadian RCT published in 2008[13] added further support for breathing retraining in asthma, also finding significant reductions in asthma symptoms. In this study, a breathing retraining intervention delivered by physiotherapists in a face-to-face setting was compared with the Butekyo breathing method (also taught in face-to-face sessions by a therapist). Large magnitude but similar improvements in health status and symptoms from baseline levels were seen in both treatment arms.

A further RCT published in 2009 investigated the effects of a physiotherapist-delivered breathing retraining intervention, with similar content to that included in the face-to-face arm of our trial.[17] This study controlled for the non-specific 'placebo-like' effect of professional contact and sympathetic attention by giving the control group the same amount of professional contact time (with an experienced respiratory nurse providing asthma education). Significant improvements from baseline were seen in patient-reported asthma outcomes for both treatment arms after 1 month, with trends favouring the breathing retraining group; at 6 months a large and significant difference between treatment arms was found in favour of breathing retraining. Significant improvements were seen between treatment arms in asthma-related QoL, anxiety and depression and Nijmegen questionnaire scores (measuring hyperventilation-related symptoms) and a trend was seen for an improvement in symptomatic asthma control. No effect on airway inflammation or physiology was found. No economic evaluation was carried out.

The addition of these subsequent trials to those in the Cochrane review[23] as part of the BTS review[20] led the authors to conclude that the evidence supporting breathing retraining for people with asthma was of 1++ strength. However, no recommendation on the most clinically effective or cost-effective way of providing breathing retraining was made. Most of the studies contributing to the evidence base involved face-to-face interventions and it is here that the evidence is strongest. Only two preliminary studies have investigated the use of instructional interventions delivered by videotape or DVD,[9,14] with some evidence that this modality may also be effective. To our knowledge, no previous studies have compared a DVD breathing retraining intervention with a face-to-face breathing retraining intervention. In our study we aimed to assess the effectiveness of the intervention not only in comparison with usual care or a placebo but also in comparison with an intervention of known benefit. The logistic and economic implications of making this intervention available to all who could potentially benefit in the UK through a face-to-face physiotherapy programme are considerable. We felt that if comparable effectiveness could be shown for a self-guided breathing retraining programme, this is likely to provide a more efficient, convenient and cost-effective service to patients. The available evidence prior to this study suggested that a programme of breathing retraining consisting of three or more face-to-face sessions delivered by a specialist respiratory physiotherapist was effective in improving patient-reported end points, particularly health status (the outcome measure that most accurately captures patient experiences and QoL impairment) and psychological well-being, for people with asthma, and may be effective in reducing rescue bronchodilator medication usage. There were suggestions that similar beneficial effects may be achieved through the use of self-guided interventions instead of face-to-face instruction. However, the relative clinical effectiveness and cost-effectiveness of different approaches to breathing retraining have not been adequately assessed. If similar benefits could be demonstrated without face-to-face contact with a health-care professional, the health resource implications of providing breathing retraining would be improved and this intervention could realistically be made available to the many people with asthma who could potentially benefit from it. Therefore, we proposed to transfer the key components of the physiotherapist-delivered programme that we (and others) have shown to be effective into a self-guided format (delivered in this study through a DVD, but able to be delivered through internet-based technologies) and to compare the effects of this intervention with those of face-to-face sessions with a physiotherapist and with usual care. Our study included a full health economic evaluation, as previous research has focused on the clinical effectiveness, rather than the cost-effectiveness, of breathing retraining. We also included qualitative research to capture patient perspectives on the interventions and a full process evaluation.

Chapter 2 Methods

Trial design

The BREATHE (Breathing REtraining for Asthma – Trial of Home Exercises) trial was a pragmatic, observer-blinded, three-arm, parallel-group RCT comparing breathing retraining delivered using a DVD with face-to-face physiotherapy and with usual care (control) for adults with asthma and impaired health status.

Participants

We recruited 655 adult patients with a diagnosis of asthma and impaired asthma-related health status from 34 primary care sites (UK NHS general practices) in the Wessex region. Patients were recruited between November 2012 and January 2015, with follow-up ending in February 2016. Practices were recruited and supported by the UK Clinical Research Network (CRN), who also supported patient recruitment and follow-up.

Inclusion criteria

Inclusion criteria

- Full practice registration for 12 months prior to enrolment.
- Age 16–70 years.
- Physician-diagnosed asthma in medical records.
- One or more anti-asthma medication prescriptions in the previous year (determined from physician prescribing records).
- Impaired asthma-related health status [Asthma Quality of Life Questionnaire (AQLQ)[24] score of < 5.5].
- Able to give informed consent.

Exclusion criteria

Exclusion criteria

- Asthma judged at the baseline assessment to be dangerously unstable and in need of urgent medical review (if these participants were referred back to their usual primary care clinician for review).
- Patients with an additional documented diagnosis of chronic obstructive pulmonary disease (COPD) with a forced expiratory volume in 1 second (FEV_1) of $< 60\%$ predicted.

We aimed to allow broad entry criteria (with the inclusion of smokers and not insisting on physiological demonstration of reversible airflow obstruction) to allow the generalisability of the research findings to mild-to-moderate UK asthma populations treated in primary care NHS practice.

Interventions

Development of the self-guided intervention

The development process for the self-guided intervention is described in detail in *Chapter 5*.

Briefly, in phase 1 of the study, the development phase, we transferred an existing face-to-face programme of breathing retraining taught by physiotherapists to patients with dysfunctional breathing, and previously shown to be effective for people with poorly controlled asthma, to audio-visual media (trialled in DVD

format in this study), and developed printed supportive materials and undertook qualitative piloting of these materials to optimise their acceptability and effectiveness.

Patient educational materials were developed by members of the team including physicians, physiotherapists, health psychologists, communications technology specialists and patient representatives. The DVD and accompanying booklet were created iteratively, with extensive qualitative patient input. The DVD content consisted of:

- a detailed explanation and illustration of how to carry out the exercises
- motivational components explaining the rationale for the exercises and addressing common doubts and concerns.

The materials were piloted with a panel of 29 members of the target population, purposively sampled for diversity in terms of age, sex, education and symptom profile. In audio-recorded face-to-face and telephone interviews we used open-ended questions to explore attitudes to the proposed treatment method in the context of health beliefs and then used 'think-aloud' methods[12] to elicit spontaneous reactions to all of the proposed materials. We modified the scripts based on this feedback. Professional production of the DVD and booklet were undertaken and the materials were reviewed by members of our panel, who provided final feedback in face-to-face and telephone interviews.

Face-to-face physiotherapy

Participants randomised to the face-to-face physiotherapy arm were treated by a single, very experienced respiratory physiotherapist over three sessions, based on the face-to-face breathing retraining interventions studied in previous research and on the standard Papworth breathing retraining programme widely taught by physiotherapists in the UK and globally.[17–19] The content of the programme was very similar to that in the DVD arm of the study. The patient support booklet produced in the development phase to support the DVD-based breathing retraining, as described in the previous section, was also provided to patients in this arm of the study. The details and fidelity assessment of the physiotherapy intervention are described in more detail in *Chapter 5*.

Control group

Patients randomly assigned to the control arm (usual care) received no additional treatment or care. They underwent the same baseline and 12-month assessments and completed the 3- and 6-month postal questionnaires. Control participants were informed that they would subsequently be offered the DVD intervention if it was shown to be effective in the study, to encourage participation and retention.

Randomised controlled trial processes

We performed a parallel-group, three-arm RCT over a 12-month period to assess the effect of the DVD programme compared with usual care and face-to-face physiotherapist-led training with a similar content on the following parameters: asthma-related health status, parameters of symptomatic and physiological asthma control and asthma-related health resource use. Consenting participants were randomly assigned to (1) receipt of the DVD intervention plus supporting written material, (2) three sessions of face-to-face physiotherapy breathing instruction, consisting of an initial 'small-group' (up to five patients) session of approximately 45 minutes and two subsequent individual sessions of up to 45 minutes or (3) usual care, which included recruitment and follow-up assessments but no additional intervention or care.

Identification, recruitment and randomisation of participants

Potentially eligible patients in the participating practices were identified by searches of the practice computerised clinical record and prescribing systems. The searches were facilitated by the CRN, based on the inclusion criteria described earlier. Potentially eligible participants were sent information about the study, an AQLQ questionnaire to complete and return if interested in participating and a stamped return envelope. Contact telephone numbers were provided for patients who wished to discuss the study.

Those returning information and interested in participating in the study and who met the inclusion criteria were seen by one of the study research nurses [from the CRN Primary Care Research Network (PCRN) team] at their own general practice during a prearranged appointment. Patients who met the inclusion criteria at the research nurse review and who still wanted to participate provided written informed consent, had baseline measurements taken and were randomly allocated to one of the three study arms following a telephone call to the randomisation service of the Southampton Clinical Trials Unit (SCTU). Follow-up and intervention arrangements were made according to participant convenience and availability. All participants were informed that they would receive postal questionnaires to complete and return at 3 and 6 months, and would be invited for a further research nurse appointment at 12 months. Usual care for their asthma was otherwise allowed to continue.

DVD arm

Participants allocated to the DVD arm received a copy of the self-guided programme in DVD format and the printed support booklet. To cover the possibility of lack of access to a DVD player we were able to provide an inexpensive DVD player for participant use; however, none of the participants allocated to the DVD arm required this.

Physiotherapy arm

Those allocated to the face-to-face physiotherapy arm consented to be contacted by the physiotherapist delivering the intervention by telephone within the following week to arrange the first session. This took place at their general practice at a mutually convenient time. Subsequent sessions were arranged during the first session.

Usual-care arm

Participants in the control arm received no additional information or care during the study beyond their usual care.

Postal questionnaire

The AQLQ questionnaires were posted to all participants at 3 and 6 months after baseline along with a prepaid return envelope. A single reminder telephone call was made after 4 weeks.

Final visit

All participants were invited to a final study visit with a blinded research nurse (a different research nurse from the research nurse who carried out the baseline assessments) at their usual general practice 12 months after baseline. All baseline physiological and questionnaire measurements were repeated. Process evaluation questionnaires were completed and information on personal costs was collected. Participants who did not attend were sent a reminder and, if they were unwilling or unable to attend for a face-to-face visit but were willing to answer questions over the telephone, the AQLQ was completed to allow maximum collection of the primary efficacy outcome.

Health resource use

Health resource use information was extracted from medical records for all participants following the 12-month assessment. This included all respiratory-related medical encounters (primary and secondary care), investigations relating to asthma and respiratory-related prescribing.

Outcomes

Prespecified outcome measures were between-group and within-group changes from baseline to the end of the study (12 months). The statistical analysis plan (SAP) is provided below (see *Statistical analysis plan*).

The primary outcome was the between-group [intention-to-treat (ITT) population] change in asthma-specific health status [AQLQ (short version)] score, adjusted for potential confounders.

Secondary outcome measures were between-group (ITT population) change in Asthma Control Questionnaire (ACQ)[25] score, lung function [FEV_1, forced volume vital capacity (FVC), FEV_1-to-FVC ratio, peak expiratory flow rate (PEFR)], fraction of exhaled nitric oxide (FeNO), health status [EuroQol-5 Dimensions (EQ-5D)[26]], anxiety and depression [Hospital Anxiety and Depression Scale (HADS)[27]], hyperventilation (Nijmegen) questionnaire[28] score, oral corticosteroid courses for asthma exacerbations and bronchodilator use.

Sensitivity analyses included analyses of the primary and secondary outcomes in both the ITT and per-protocol (PP) populations. We also performed a prespecified sensitivity analysis including participants with missing baseline or outcome data for the primary efficacy parameter, the AQLQ, as described below and in the SAP. In addition, health economic and process evaluation analyses were carried out and are presented in *Chapters 4* and *6* respectively.

Sample size

For equivalence of the DVD-delivered and face-to-face programmes

In a previous Health Technology Assessment (HTA) study,[29] treatments were deemed to be equivalent if the 95% confidence interval (CI) for the mean difference in AQLQ score between treatment arms was wholly included between –0.3 and +0.3. The BREATHE sample size calculation for equivalence used the same equivalence boundary (i.e. between –0.3 and +0.3). However, we assumed that the standard deviation (SD) of the between-group difference in AQLQ score would be a conservative 25% smaller (i.e. SD 0.77) than that reported in a previous study (SD 1.03).[18] The justification for this was that the proposed equivalence analysis compared two breathing retraining interventions as opposed to a breathing intervention compared with usual care, as in the GLAD study. As this was an equivalence study, as opposed to a non-inferiority study, a two-tailed 5% significance level was used in the calculations.

Sample sizes of 210 in the DVD breathing retraining group and 105 in the face-to-face physiotherapy group were required to assess treatment equivalence with 90% power using an equivalence boundary for AQLQ score of 0.3. This assumed that the expected between-group difference in mean AQLQ score was zero; a two-tailed 5% significance level; a common SD for the AQLQ score of 0.77; and a lower/upper limit of –0.3/+0.3 for the 95% CI of the between-group difference in AQLQ score.

In the unlikely event that the between-group AQLQ score SD was higher than our estimated 0.77, assuming that all other parameters stayed the same, we would still have 80% power to declare equivalence between the DVD breathing retraining group and the face-to-face physiotherapy group as long as the between-group SD was no higher than 0.89.

For superiority of both the DVD-delivered and the face-to-face programme over usual care

For the superiority sample size calculations, there was no widely acceptable minimal clinically important difference (MCID) for between-group change in AQLQ score, although the MCID for within-person change in AQLQ score was reported to be 0.5 (SD 0.41).[24] Therefore, two approaches were used for the superiority sample size calculation: (1) using the published within-person MCID of 0.5 and (2) using the estimate from the previous study[18] – a between-group mean (SD) difference in AQLQ score at 6 months of 0.38 (1.03). Although the original sample size calculations for the superiority study were carried out using a one-sided 5% significance level, subsequent open discussions between the trial team and the Data Monitoring and Ethics Committee (DMEC) and the Trial Management Group (TMG) resulted in a protocol change and the

decision to use a two-sided 5% significance level. The following superiority study sample size calculations have been updated to reflect this change:

1. *Using a MID of 0.5*. A two-group *t*-test with a two-sided 5% significance level will have 90% power to detect a difference in mean AQLQ score of ≥ 0.5, assuming that the common SD is 0.41, when the sample sizes are 12 in the face-to-face breathing retraining group and 24 in the usual-care group. Similarly, a two-group *t*-test with a two-sided 5% significance level will have 90% power to detect a difference in mean AQLQ score of ≥ 0.5, assuming that the common SD is 0.41, when the sample size is 16 in both the DVD-delivered breathing retraining group and the usual-care group.
2. *Using a MID of 0.38*. A two-group *t*-test with a two-sided 5% significance level will have 90% power to detect a difference in mean AQLQ score of ≥ 0.38, assuming that the common SD is 1.03, when the sample sizes are 117 in the face-to-face breathing retraining group and 234 in the usual-care group. Similarly, a two group *t*-test with a two-sided 5% significance level will have 90% power to detect a difference in mean AQLQ score of ≥ 0.38, assuming that the common SD is 1.03, when the sample size is 156 in both the DVD-delivered breathing retraining group and the usual-care group.

Final sample size

Assuming a 10% dropout rate and a two-sided 5% significance level for each of the equivalence and superiority studies, we therefore aimed to recruit a total sample size of 650 patients (260 each in the DVD and usual-care arms and 130 in the face-to-face physiotherapy arm).

Changes to the original protocol

There were two significant amendments to the original protocol developed in 2012. There was concern from the DMEC that the attrition rate may be higher than the 10% initially anticipated. The protocol was subsequently amended to allow recruitment to be extended to ensure that the original target of 525 complete data sets was reached.

The second noteworthy amendment was to the hypothesis tests of the statistical analysis. The decision was made to change the trial's superiority sample size calculations from a one-sided 5% analysis to a two-sided 5% analysis. The trial was adequately powered for either option but, after extensive discussions with the funder, sponsor, Trial Steering Committee (TSC), TMG and DMEC, it was agreed that the use of a two-sided sample size calculation would be optimum.

Statistical analysis plan

Statistical analysis plan objective

The objective of this SAP is to describe the quantitative statistical analyses to be carried out for the equivalence and superiority studies within BREATHE. This SAP is based on protocol version 7 (25 November 2015).

General principles

Categorical variables will be described with number and percentage in each category. Continuous variables will be described with mean and SD or median and interquartile range (IQR) depending on their distribution. The number of missing data will be provided for each variable.

Software

All analyses will be carried out using Stata® version 14 (StataCorp LP, College Station, TX, USA) or SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). Data will be stored on a secure drive, with limited access to those who need it.

Study populations

All primary efficacy analyses are carried out on the ITT population. Safety analyses are carried out on the safety population.

Intention-to-treat population

All participants who were randomised and for whom at least one follow-up observation of the primary outcome (AQLQ score) is available. Participants will be analysed in the treatment arm to which they were randomised.

Per-protocol population

All participants of the ITT population excluding participants who were not compliant with their randomised study arm. Non-compliance is defined as those not having any primary outcome data and/or those not attending at least two physiotherapy appointments in the physiotherapy arm.

Effectiveness outcomes

Primary outcome

The primary outcome measure will be the 12-month post-intervention AQLQ score.

Secondary outcomes

Clinical

- ACQ score.
- Lung function (FEV_1, FEV_1-to-FVC ratio, PEFR).
- FeNO.
- Health status (EQ-5D).
- Anxiety and depression scores (HADS questionnaire).
- Hyperventilation (Nijmegen) questionnaire.
- Oral corticosteroid courses.
- Bronchodilator use.
- Smoking status.
- Process evaluations.
- Patient-reported process evaluations (qualitative).

Engagement

- Estimates of engagement with use of physiotherapy exercises in the physiotherapy arm.
- Estimates of engagement with the breathing retraining.

Economic

- Quality-adjusted life-years (QALYs).
- Asthma-related health resource use.
- Cost-effectiveness/utility.

Safety outcomes

- Serious adverse events.
- Non-serious adverse events.
- Suspected unexpected serious adverse reactions.

Analysis

General principles

For the equivalence study, the adjusted repeated-measures mixed-model ITT analysis will be deemed the primary analysis with an adjusted repeated-measures mixed-model per-protocol analysis as a sensitivity analysis. For the superiority study, in accordance with Consolidated Standards of Reporting Trials (CONSORT) guidelines, all comparative analysis will be conducted on an ITT repeated-measures mixed-model basis with a per-protocol repeated-measures mixed-model analysis performed as a sensitivity analysis. All analyses will be governed by this comprehensive SAP which will be agreed by the TSC and approved by the independent DMEC prior to any analyses being undertaken. There will be no formal interim analyses undertaken. Unless prespecified, a 5% two-sided significance level will be used to denote statistical significance throughout. As we specify a clear sequence of tests with a priori effect sizes to inform treatment selection, no adjustments will be made for multiple testing.

Data description

All variables will be described for each treatment group separately and for all participants together. This will be the number and percentage within each category for binary and categorical variables. Continuous variables will be described using the mean and SD (if normally distributed) or median (IQR) if skewed.

Missing data

A CONSORT flow diagram will provide the detail of the flow of trial participants, withdrawals and post-randomisation exclusions.

Missing baseline data

As this is collected at clinic by the research nurse it is anticipated that missing baseline data will be minimal (< 10%). Missing baseline data will be reported in the form of the number and percentage [*n* (%)] by variable and by randomised group. If a baseline variable has more than 10% missing data, we will use the missing indicator method recommended by White and Thompson.[30] This method is deemed a good approach irrespective of whether any missing baseline data does or does not predict the outcome. For missing baseline AQLQ scores, the method specified in Juniper *et al.*[24] was adopted. Values for each domain were calculated provided at least two-thirds of the items were scored; otherwise the domain value was set to missing. If any domain score was missing the overall AQLQ score was set to missing.

(a) *Missing primary outcome data*. The repeated-measures mixed-model approach will account for missing data as long as at least one assessment of outcome is available. Compared to analysis of covariance (ANCOVA), a mixed-model approach is thought to give a more precise estimate of treatment effect at the final time point. Participants who do not provide any primary outcome follow-up data will therefore be excluded from the analysis. However, a prespecified sensitivity analysis will be carried out to include all randomised participants using the strategy reported by White *et al.*[31] This involves substituting the missing baseline AQLQ score by the specific trial arm mean and for missing 12-month AQLQ scores the method of last observation carried forward (LOCF) will be applied. If 12-month value is missing, the 6-month AQLQ score will be used to replace. If both 12-month and 6 month are missing, the 3-month AQLQ score will be used to replace the 12-month score. If all 3-month, 6-month and 12-month are missing, i.e. no follow-up information is available, then it will be assumed that the patient returned to their baseline AQLQ value.

(b) *Missing secondary outcome data*. The number of baseline missing data per secondary outcome will be reported per randomised group and overall. Secondary outcomes analysed by repeated-measures mixed-effects models will assume missing at random. If this assumption is thought to be violated, we will consider alternative modelling strategies such as pattern mixture models.

Analysis of the primary outcome

Equivalence study

A 95% CI will be constructed for the mean difference in 12-month total AQLQ score between the DVD arm and the 'face-to-face' breathing retraining arm. Since the equivalence boundary is set at 0.3, equivalence will be declared if the 95% CI is wholly included between –0.3 and +0.3. If equality is not evident, then a repeated-measures mixed-model will be used to examine whether the 'face-to-face' breathing retraining arm is superior to the DVD arm via examination of the difference (and 95% CI) of 12-month total AQLQ score (and each of the four domain scores) before and after adjustment for baseline AQLQ score and a set of prespecified variables. The prespecified variables are AQLQ score at baseline and the fixed effects of treatment arm, time, arm by time interaction plus the random effects of general practice and the patient-level covariates of age, sex, smoking status, BTS treatment step, baseline HADS score and baseline Nijmegen score. Correlations between baseline variables will be explored for the overall population on unblinded data and, if collinearity is evident, the most appropriate variables will be included in the final model. Models with different covariance assumptions were compared by using the Akaike information criterion (AIC); changes at 12 months between physiotherapy vs. usual care; DVD vs. usual care; DVD vs. physiotherapy were estimated from these models. Results from the adjusted ITT repeated-measures mixed model are deemed the primary analyses.

For participants that are lost to follow-up at some time during the 12-month follow-up their information will be included in the statistical analysis up to the point that they are lost to follow-up. The mixed-effects model assumes that data are missing at random and allows for unbalance or missing observations within subject.

Superiority study

Baseline comparability between the three arms of the trial will be evaluated by examination of summary statistics (the mean and SD or median and IQR for continuous variables, dependent on their distribution, and the number and percentage for categorical variables). In accordance with CONSORT guidelines, all comparative analysis will be conducted on an ITT basis with a per-protocol analysis performed as a sensitivity analysis.

For the primary outcome, a repeated-measures mixed model will be used to examine the 12-month total AQLQ score (and each of the four domain scores) across the three arms with adjustment for baseline AQLQ score and a set of prespecified variables. The same model procedure used in the equivalence study will be adapted here. Pairwise comparisons of AQLQ differences will be examined between the 'usual-care' arm and each of the DVD and 'face-to-face' breathing retraining arms via calculation of two sided 95% CIs. If the CI includes +0.3 then superiority of either the DVD or 'face-to-face' breathing retraining arms over usual care will be rejected.

Analysis of secondary outcomes

Equivalence study

A repeated-measures mixed model will be used to analyse the difference (and 95% CI) for the secondary outcome measures (ACQ, EQ-5D, HADS score) at 12 months before and after adjustment for baseline values and a set of prespecified variables. The list of prespecified variables is general practice (as a random effect), age, sex, smoking status, BTS treatment step, baseline HADS score and baseline Nijmegen score. For those secondary outcomes collected only at baseline and 12 months' follow-up such as lung function, FeNO, Nijmegen score, ANCOVA will be used to analyse 12-month group differences before and after adjustment for baseline values and a set of aforementioned prespecified variables.

For those secondary outcomes that involve count data (i.e. oral corticosteroid courses, bronchodilator use, asthma-related health-care resource use), Poisson regression analysis (or negative binomial regression on failure of the assumptions of Poisson regression) with a log link function will be performed to give rate ratios (and their 95% CIs) in the DVD and 'face-to-face' breathing retraining arm both before and after adjustment for prespecified variables of general practice, age, sex, smoking status, BTS treatment step, baseline HADS score and baseline Nijmegen score. The exact number of covariates that will be included in the adjusted model will be dependent on the distribution of the secondary outcome and avoidance of loss of power.

Superiority study

A repeated-measures mixed model will be used to analyse the continuous secondary outcome measures [ACQ, EQ-5D and HADS score (both anxiety and depression scores)]. The 'usual-care' arm will be compared with each of the DVD and 'face-to-face' breathing retraining arms in turn.

For those secondary outcomes collected only at baseline and 12 months' follow-up, such as lung function, FeNO and Nijmegen score, ANCOVA will be used to analyse 12-month group differences before and after adjustment for baseline values and a set of aforementioned prespecified variables.

For those secondary outcomes that involve count data (i.e. oral corticosteroid courses, bronchodilator use, asthma-related health-care resource use), Poisson regression (or negative binomial regression on failure of the assumption of Poisson regression) with a log link function will be performed to give rate ratios (and their 95% CIs) in the DVD and 'face-to-face' breathing retraining arm compared with 'usual care' both before and after adjustment for list of prespecified variables such as general practice, age, sex, smoking status, BTS treatment step, baseline HADS score and baseline Nijmegen score. The exact number of covariates that will be included in the adjusted model will be dependent on the distribution of the secondary outcome and avoidance of loss of power.

Engagement

The proportion (*n*) of participants who attended none, one, two and all three physiotherapy sessions in the physiotherapy arm will be tabulated.

Primary and secondary efficacy (equivalence study) analyses relating to the AQLQ (and each of the four domain scores) at 3 and 12 months will be repeated as a sensitivity analyses in two ways:

1. *Engagement*. Participants who did not engage with the breathing retraining at 3 months will be excluded. Engagement will be included as a binary variable defined by any response above 'never started' to any of the first three questions (number of weeks, days per week and times per day) in the 'carrying out the breathing retraining' block of treatment engagement questions at 3 months.
2. *Amount of practice*. Participants who did not engage with the breathing retraining at 3 months will be excluded and a new covariate – the amount of practice undertaken – will be added to the models. Amount of practice is a continuous variable which will be calculated by multiplying weights from each of the three questions shown in *Table 1*.

TABLE 1 Questionnaire used to quantify amount of practice

Question	Response	Score	Example
Q1. For how many weeks did you carry out the breathing retraining?	Never started	0	If a participant carried out breathing retraining for 3–5 weeks, for 3–4 days at least twice a day, this would be a score of 32 (4 × 4 × 2) for the number of practice sessions completed
	1 week	1	
	1–2 weeks	2	
	3–5 weeks	4	
	6–8 weeks	7	
	≥ 9 weeks	10	
Q2. How many times a week, on average, did you carry out the breathing retraining?	Never started	0	
	1–2 days	2	
	3–4 days	4	
	5–6 days	6	
	Most days	7	
Q3. How many times a day, on average, did you carry out the breathing retraining?	Never started	0	
	Once a day	1	
	At least twice a day	2	

Note
Incongruent responses across the three questions (e.g. if a participant gives a response of 1 week for Q1 and a response of never started for Q2 and Q3) will be reviewed individually for coding. However, it is anticipated that responses will be rounded up to the next lowest response (e.g. a response of 1 week for Q1 and a response of never started for Q2 and Q3 will be rounded up from 1 × 0 × 0 to be given a score of 1 × 2 × 1 = 2).

Chapter 3 Results

Recruitment

We recruited patients from 34 primary care sites in Wessex through the PCRN (subsumed during the study into the CRN). We identified potential recruits to the study by searching general practice electronic medical records for patients with a coded diagnosis for asthma, undergoing current treatment and meeting inclusion criteria. Potential recruits were sent information about the study, the AQLQ (as impaired disease-specific health status was an inclusion criteria to enable an improvement to be demonstrated) and a prepaid return envelope.

A total of 15,203 invitation letters were mailed to potential participants and 1481 responses were received (a response rate of 9.7%). In total, 680 (45.9%) respondents were deemed ineligible, with lack of impairment according to AQLQ score being the most common reason for ineligibility; 655 participants (81.8% of the eligible respondents) were randomised, 261 (39.8% of randomised participants) to the DVD-delivered breathing retraining group, 262 (40.0%) to the usual-care group and 132 (20.2%) to the physiotherapist breathing retraining group (*Table 2*). The numbers of patients randomised from the different practices are shown in *Appendix 1*. The CONSORT diagram showing the flow of participants through the trial is provided in *Figure 1*.

Because of errors in completion of the primary outcome (AQLQ) at baseline for 45 out of 655 participants (7%), it was not possible to assign an AQLQ score to these patients. However, one or more AQLQ returns was achieved for all randomised participants.

Baseline characteristics and demographics

Baseline demographic and clinical features of the participants in the study are shown in *Table 3*. The demographic and clinical profiles of the recruited population were typical of adult patients with mild-to-moderate asthma in the community and were similar between treatment arms. More women than men consented to participate in the trial and the median age of participants was 57 years, with approximately one-third of participants aged < 50 years. The median (IQR) age at diagnosis of asthma was 29 (11–45) years. In total, 8% of participants were current smokers and 33% were ex-smokers. Approximately one-third of participants had a family history of asthma. The most common self-reported asthma triggers were dust (77%), pollen (64%), smoke (64%), exercise (63%), stress (46%), cats (41%), dogs (24%) and food (19%).

Participants had mildly impaired lung function, with a mean FEV_1% predicted of 91% and a mean FEV_1-to-FVC ratio of 0.8. The median (IQR) FeNO, a measure of eosinophilic airway inflammation, was 22 (14–34) parts per billion, which is at the top end of the normal range; over one-quarter of participants had a raised reading, indicative of persisting active inflammation despite inhaled steroid treatment. In terms of the BTS treatment step, our patient sample was typical of adult asthma patients treated in the community,

TABLE 2 Numbers of patients randomised and in the ITT and PP populations, overall and by treatment arm

	Treatment arm, *n*			
Population	DVD	Physiotherapy	Usual care	Overall, *n*
ITT	261	132	262	655
PP	215	110	231	556

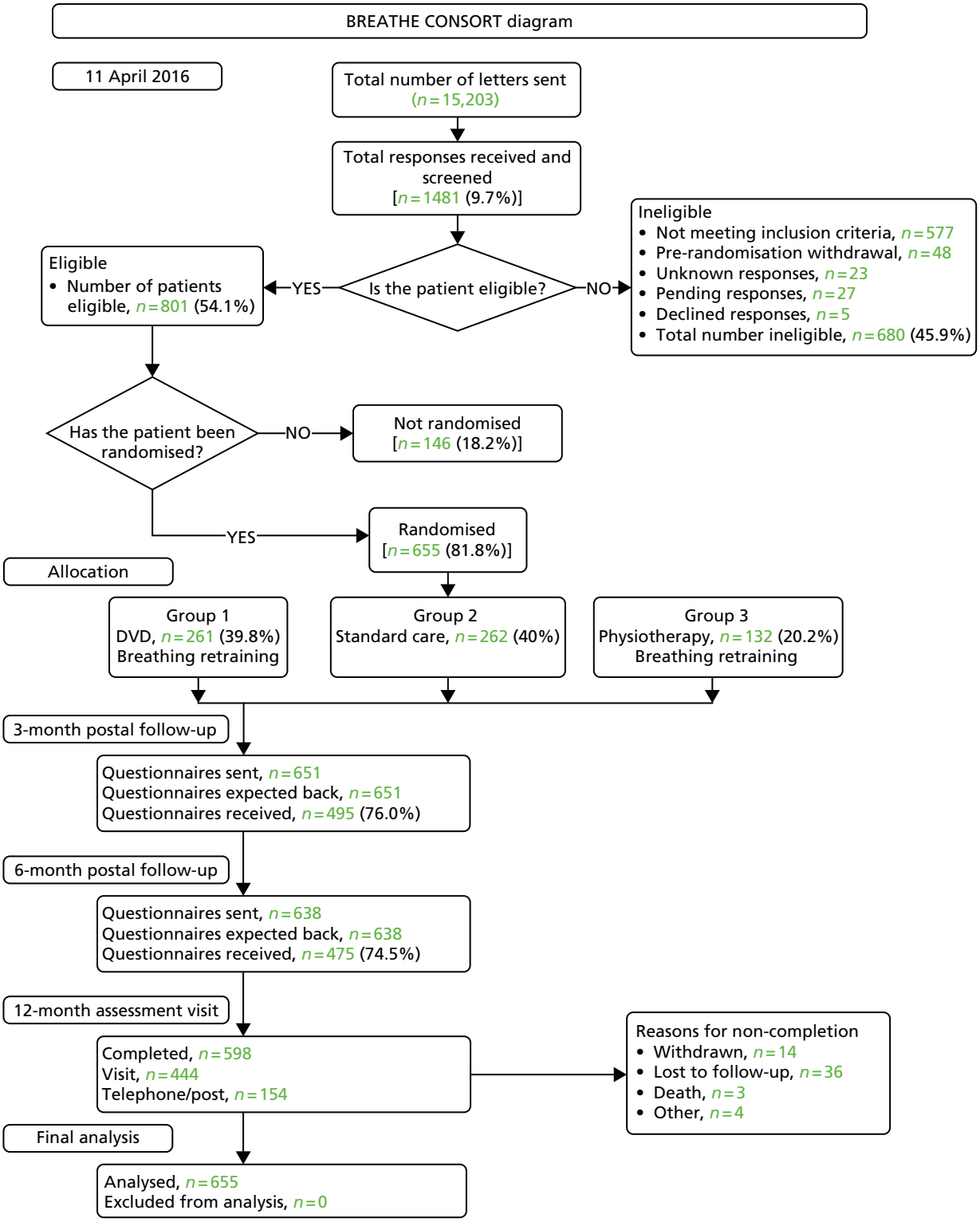

FIGURE 1 Consolidated Standards of Reporting Trials diagram.

with 7% at step 1 (needing short-acting beta-agonists only), 27% at step 2, 42% at step 3 and 12% at step 4 or 5. Self-reported atopic comorbidity was common (*Table 4*), with approximately two-thirds of participants reporting allergic problems including allergic rhinitis (69%) and eczema (31%), with most requiring pharmacological treatment. Over one-third of participants reported psychological problems (anxiety and depression), again with most requiring medication. Diagnosed COPD was present in only 2% of participants and had to be mild to meet entry criteria.

TABLE 3 Baseline characteristics of participants by treatment arm

Characteristic	Treatment arm			Overall (*N* = 655)
	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	
Sex, *n* (%)				
Male	97 (37.2)	41 (31.1)	98 (37.4)	236 (36.0)
Female	164 (62.8)	91 (68.9)	164 (62.6)	419 (63.9)
Age (years), median (IQR)	56 (45–65)	55 (47–63)	57 (47–65)	57 (46–64)
Age group (years), *n* (%)				
≤ 40	47 (18.0)	21 (15.9)	43 (16.4)	111 (16.9)
41–50	54 (20.7)	28 (21.2)	45 (17.2)	127 (19.4)
51–60	59 (22.6)	35 (26.5)	73 (27.9)	167 (25.5)
> 60	101 (38.7)	48 (36.4)	101 (38.5)	250 (38.2)
Weight (kg)				
Number included	258	132	261	651
Mean (SD)	79.9 (17.6)	80.6 (20.2)	83.1 (18.1)	81.3 (18.4)
Height (cm)				
Number included	258	132	261	651
Mean (SD)	167.1 (9.0)	165.7 (8.8)	166.1 (9.1)	166.4 (9.0)
Smoking status, *n* (%)				
Current smoker	16 (6.1)	13 (9.8)	21 (8.0)	50 (7.6)
Ex-smoker	74 (28.4)	43 (32.6)	102 (38.9)	219 (33.4)
Never	169 (64.8)	76 (57.6)	139 (53.1)	384 (58.6)
What they currently smoke, *n* (%)				
Cigarettes	10 (3.8)	8 (6.1)	15 (5.7)	33 (5.0)
Tobacco	6 (2.3)	5 (3.8)	7 (2.7)	18 (2.7)
Cigars	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.2)
Cigarettes/tobacco	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)
Tobacco/cigars	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.2)
What they used to smoke, *n* (%)				
Cigarettes	69 (26.4)	40 (30.3)	96 (36.6)	205 (31.3)
Tobacco	6 (2.3)	4 (3.0)	8 (3.1)	18 (2.7)
Cigars	3 (1.1)	3 (2.3)	1 (0.4)	7 (1.1)
Cigarettes/tobacco	2 (0.8)	1 (0.8)	2 (0.8)	5 (0.8)
Tobacco/cigars	1 (0.4)	1 (0.8)	0 (0.0)	2 (0.3)
Cigarettes/cigars	2 (0.8)	2 (1.5)	1 (0.4)	5 (0.8)
Cigarettes/tobacco/cigars	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.2)

continued

TABLE 3 Baseline characteristics of participants by treatment arm (*continued*)

Characteristic	Treatment arm			Overall (*N* = 655)
	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	
Average number of cigarettes per day for ever smokers				
Number included	78	47	111	236
Median (IQR)	20 (10–21)	15 (10–20)	15 (6–20)	15 (8–20)
Minimum, maximum	1, 80	3, 60	1, 100	1, 100
Pack-years of smoking among ever smokers				
Number included	82	49	113	244
Median (IQR)	15 (5–30)	13 (3–27)	10 (3–23)	12 (3–25)
Minimum, maximum	0.05, 112.5	0.25, 159	0.05, 300	0.05, 300
Age diagnosed with asthma (years)				
Number included	259	132	259	650
Median (IQR)	27 (12–45)	32 (14–45)	28 (8–46)	29 (11–45)
Family history of asthma, *n* (%)				
Mother				
Yes	35 (13.4)	28 (21.2)	43 (16.4)	106 (16.2)
No	220 (84.3)	99 (75.0)	212 (80.9)	531 (81.1)
Unknown	2 (0.8)	4 (3.0)	7 (2.7)	13 (2.0)
Father				
Yes	31 (11.9)	17 (12.9)	26 (9.9)	74 (11.3)
No	218 (83.5)	108 (81.8)	219 (83.6)	545 (83.2)
Unknown	8 (3.1)	6 (4.6)	17 (6.5)	31 (4.7)
Siblings				
Yes	67 (25.7)	35 (26.5)	61 (23.3)	163 (24.9)
No	180 (69.0)	84 (63.6)	176 (67.2)	440 (67.2)
n/a	7 (2.7)	13 (9.9)	23 (8.8)	43 (6.6)
Children				
Yes	85 (32.6)	38 (28.8)	83 (31.7)	206 (31.5)
No	125 (47.9)	66 (50.0)	129 (49.2)	320 (48.9)
n/a	48 (18.4)	27 (20.5)	50 (19.1)	125 (19.1)
Other family members				
Yes	87 (33.3)	50 (37.9)	94 (35.9)	231 (35.2)
No	159 (60.9)	76 (57.6)	159 (60.7)	394 (60.2)
Unknown	5 (1.9)	3 (2.3)	4 (1.5)	12 (1.8)
Asthma triggers, *n* (%)				
Cats	119 (45.6)	60 (45.5)	109 (41.6)	288 (43.9)
Dogs	68 (26.1)	37 (28.0)	73 (27.9)	178 (27.2)
Dust	214 (81.9)	108 (81.8)	215 (82.1)	537 (81.9)
Exercise	185 (70.9)	100 (75.8)	191 (72.9)	476 (72.7)

TABLE 3 Baseline characteristics of participants by treatment arm (*continued*)

Characteristic	Treatment arm			Overall (*N* = 655)
	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	
Pollen	164 (62.8)	89 (67.4)	177 (67.6)	430 (65.7)
Smoke	186 (71.3)	97 (73.5)	174 (66.4)	457 (69.8)
Stress	133 (50.9)	67 (50.8)	133 (50.8)	333 (50.8)
Food	42 (16.1)	33 (25.0)	58 (22.1)	133 (20.3)
Other	211 (80.8)	92 (69.7)	198 (75.6)	501 (76.5)
FeNO (p.p.b.)				
Number included	238	126	242	606
Median (IQR)	21 (14–35)	23 (15–23)	23 (14–34)	22 (14–34)
FEV_1 (l)				
Number included	246	130	253	629
Mean (SD)	2.6 (0.8)	2.5 (0.7)	2.6 (0.8)	2.6 (0.8)
FVC (l)				
Number included	246	130	253	629
Mean (SD)	3.5 (0.9)	3.3 (0.9)	3.4 (0.9)	3.4 (0.9)
FEV_1-to-FVC ratio				
Number included	246	130	253	629
Mean (SD)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)
FEV_1% predicted				
Number included	246	130	253	629
Mean (SD)	90.5 (18.8)	88.8 (18.1)	91.9 (21.6)	90.7 (19.8)
PEFR (l/second)				
Number included	244	129	249	622
Mean (SD)	425.5 (115.8)	414.9 (110.0)	423.4 (120.7)	422.5 (116.5)
BTS treatment step,[a] *n* (%)				
1	19 (7.3)	8 (6.1)	20 (7.6)	47 (7.2)
2	65 (24.9)	41 (31.1)	69 (26.3)	175 (26.7)
3	107 (41.0)	52 (39.4)	117 (44.7)	276 (42.1)
4	26 (10.0)	16 (12.1)	33 (12.6)	75 (11.5)
5	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)
Unknown/unspecified	44 (16.9)	15 (11.4)	22 (8.4)	81 (12.4)

n/a, not applicable; p.p.b., parts per billion.

a The variable BTS treatment step is derived from a medical notes review at 12 months, not at baseline. To be able to include BTS treatment step as a covariate in the adjusted analyses, a category of 'unknown/unspecified' was created to account for all patients.

TABLE 4 Self-reported comorbidities and other regular medication use at baseline by treatment arm

Comorbidity	Treatment arm			Overall (*N* = 655)
	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	
Allergies				
Yes, *n* (%)	179 (68.6)	81 (61.4)	177 (67.6)	437 (66.7)
If yes, on current medication, *n*	179	81	175	435
Unknown, *n*	4	2	3	9
Hay fever/rhinitis				
Yes, *n* (%)	183 (70.1)	94 (71.2)	174 (66.4)	451 (68.9)
If yes, on current medication, *n*	183	94	173	450
Unknown, *n*	3	0	8	12
Eczema				
Yes, *n* (%)	75 (28.7)	46 (34.8)	80 (30.5)	201 (30.7)
If yes, on current medication, *n*	75	46	78	199
Unknown, *n*	2	4	3	9
Heart disease				
Yes, *n* (%)	19 (7.3)	13 (9.8)	22 (8.4)	54 (8.2)
If yes, on current medication, *n*	19	13	22	54
Unknown, *n*	2	1	3	6
Depression/anxiety				
Yes, *n* (%)	92 (35.2)	50 (37.9)	91 (34.7)	233 (35.6)
If yes, on current medication, *n*	92	50	90	232
Unknown, *n*	1	0	1	2
Documented diagnosis of COPD				
Yes, *n* (%)	2 (0.8)	2 (1.5)	11 (4.2)	15 (2.3)
No, *n* (%)	259 (99.2)	130 (98.5)	251 (95.8)	640 (97.7)

Baseline questionnaire data (*Table 5*) showed moderate impairment in asthma-specific QoL, with a mean (SD) AQLQ score of 4.3 (0.9), and also impaired symptomatic asthma control, with a mean (SD) ACQ score of 1.5 (0.9). The baseline psychological assessment with the HADS questionnaire showed a median (IQR) anxiety score of 6 (4–9) and depression score of 3 (1–5). A score of ≤ 7 on this tool is considered 'normal' and so > 255 patients had scores suggestive of significant anxiety, in keeping with population-based survey data. Across the five domains of the EQ-5D generic QoL questionnaire, 42% of participants reported problems with pain or discomfort, 31% with activities, 27% with anxiety or depression, 23% with mobility and 5% with self-care.

In summary, we successfully recruited a population of primary care asthma patients with mild-to-moderate asthma and with evidence of incomplete asthma control and QoL impairment, our target group. Their demographic profile was similar between randomisation arms and appears to be typical of the demographic and disease control profile of UK primary care adult asthma populations reported in recent surveys of asthma control.

TABLE 5 Baseline questionnaire assessments by treatment arm

Questionnaire	Treatment arm			Overall
	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	(*N* = 655)
Mini AQLQ				
n	244	120	246	610
Mean (SD) score	4.3 (0.9)	4.2 (0.9)	4.3 (0.9)	4.3 (0.9)
Nijmegen questionnaire				
n	259	132	262	653
Mean (SD) score	19.0 (8.8)	19.0 (10.5)	19.4 (9.4)	19.2 (9.4)
HADS				
n	257	131	261	649
Anxiety, median (IQR) score	7.0 (4–8)	6.0 (4–9)	6.0 (4–9)	6.0 (4–9)
Depression, median (IQR) score	3.0 (1–5)	2.0 (1–5)	3.0 (1–5)	3.0 (1–5)
EQ-5D				
Mobility				
n	259	132	262	653
No problems, *n* (%)	202 (78.0)	97 (73.5)	203 (77.5)	502 (76.9)
Some problems, *n* (%)	57 (22.0)	35 (26.5)	59 (22.5)	151 (23.1)
Self-care				
n	258	131	262	651
No problems, *n* (%)	251 (96.3)	120 (91.6)	246 (93.9)	617 (94.8)
Some problems, *n* (%)	7 (2.7)	11 (8.4)	16 (6.1)	34 (5.2)
Usual activities				
n	259	132	262	653
No problems, *n* (%)	186 (71.8)	82 (62.1)	183 (69.8)	451 (69.1)
Some problems, *n* (%)	73 (28.2)	50 (37.9)	79 (30.2)	202 (30.9)
Pain/discomfort				
n	259	131	261	651
No problems, *n* (%)	161 (62.2)	79 (60.3)	137 (52.5)	377 (57.9)
Some problems, *n* (%)	98 (37.8)	52 (39.7)	124 (47.5)	274 (42.1)
Anxiety/depression				
n	259	132	262	653
No problems, *n* (%)	187 (72.2)	99 (75.0)	192 (73.3)	478 (73.0)
Some problems, *n* (%)	72 (27.8)	33 (25.0)	70 (26.7)	175 (27.0)
EQ-5D VAS				
n	256	131	258	645
Median (IQR)	80 (69.3–88.8)	75 (60–85)	80 (68–89)	80 (67.5–88)
Mean (SD)	74.9 (16.8)	71.7 (19.5)	74.4 (16.9)	74.1 (17.4)

continued

TABLE 5 Baseline questionnaire assessments by treatment arm (*continued*)

Questionnaire	Treatment arm			Overall
	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	(*N* = 655)
ACQ				
n	258	132	262	652
Mean (SD)	1.5 (0.9)	1.6 (0.8)	1.5 (0.9)	1.5 (0.9)

Missing data, withdrawals and study retention

Missing baseline data (see Appendix 2*)*

Because of errors in completion of the primary outcome questionnaire (AQLQ) at baseline for 45 out of 655 participants (7%), it was not possible to assign an AQLQ score to these patients. There was a very low level of missing baseline data for the other questionnaires (< 2%).

Spirometry values (FEV_1, FVC and FEV_1-to-FVC ratio) were missing for 4% of participants, PEFR values for 5% and FeNO values for 7.5%, with similar proportions of missing data between randomisation arms.

Withdrawals

Only 21 of the 655 randomised patients withdrew from the study (3.2%), with similar withdrawal rates between the DVD (5.4%), physiotherapy (2.3%) and control (2.3%) arms. The reasons for withdrawals are provided in *Appendix 3*. The baseline characteristics of those who withdrew were similar to the baseline characteristics of the randomised population (see *Appendix 4*).

Primary outcome measure: disease-specific health status measured using the Asthma Quality of Life Questionnaire

The primary efficacy analysis was a comparison of between-group changes in AQLQ scores in the ITT population, with adjustments for prespecified covariates. Secondary analyses included an unadjusted comparison of between-group changes in AQLQ scores in the ITT population, adjusted and unadjusted comparisons of between-group changes in AQLQ scores in the PP population and analyses of the subdomains measured by the AQLQ instrument. Prespecified sensitivity analyses are also reported. We also assessed the time course of changes in AQLQ score from 3-month and 6-month AQLQ postal questionnaire data.

Table 6 presents the baseline and 12-month mean (SD) AQLQ scores and the unadjusted mean changes in AQLQ scores (with 95% CIs) in the DVD, physiotherapy and usual-care arms in the ITT and PP populations. *Table 7* presents the primary efficacy analysis, the adjusted mean difference in 12-month AQLQ scores in the DVD, physiotherapy and usual-care treatment arms in the ITT and PP populations, with comparisons between the DVD arm and the control arm and between the physiotherapy arm and the control arm (superiority analysis) and between the DVD arm and the physiotherapy arm (equivalence analysis). The total AQLQ score (the primary efficacy measure) and the scores on the four subdomains of the AQLQ (which may be analysed and compared individually, measuring symptoms, activity, emotions and environment) are presented. The time course of AQLQ score changes in the ITT and PP populations is shown in *Table 8*.

Within-group Asthma Quality of Life Questionnaire score changes

There was a large within-group change in mean AQLQ score of 1.1 from baseline to the 12-month assessment in both breathing retraining arms. There was also a smaller improvement of 0.8 in the control arm. The MCID in AQLQ score for an individual patient is 0.5 and a change of 1.0 equates to a large difference.

TABLE 6 Baseline to 12-month unadjusted changes in AQLQ scores in the DVD, physiotherapy and usual-care arms in the ITT and PP populations

	Time point, mean (SD) score								
	Baseline			12 months			Unadjusted mean difference (95% CI)		
AQLQ domain	DVD	Physiotherapy	Usual care	DVD	Physiotherapy	Usual care	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy
ITT population									
n	244	120	246	231	121	246			
Total	4.3 (0.9)	4.2 (0.9)	4.3 (0.9)	5.4 (1.1)	5.3 (1.1)	5.1 (1.2)	0.32 (0.08 to 0.56)**	0.27 (0.08 to 0.47)**	–0.04 (–0.28 to 0.20)
Symptoms	4.2 (1.0)	4.0 (1.1)	4.2 (1.1)	5.2 (1.3)	5.2 (1.1)	4.9 (1.2)	0.41 (0.13 to 0.70)**	0.24 (0.01 to 0.47)*	–0.17 (–0.45 to 0.11)
Activities	5.0 (1.4)	4.8 (1.5)	5.0 (1.3)	5.9 (1.3)	5.7 (1.4)	5.7 (1.3)	0.23 (–0.04 to 0.51)	0.23 (0.002 to 0.44)*	–0.01 (–0.29 to 0.28)
Emotion	4.0 (1.3)	4.0 (1.4)	3.9 (1.4)	5.4 (1.5)	5.5 (1.3)	5.0 (1.6)	0.42 (0.08 to 0.75)*	0.36 (0.08 to 0.63)**	–0.06 (–0.39 to 0.28)
Environment	4.0 (1.1)	3.8 (1.2)	3.9 (1.2)	5.1 (1.5)	5.0 (1.3)	4.8 (1.5)	0.28 (–0.02 to 0.57)	0.31 (0.05 to 0.56)*	0.03 (–0.27 to 0.33)
PP population									
n	215	110	231	215	110	231			
Total	4.3 (0.9)	4.2 (0.9)	4.3 (0.9)	5.4 (1.2)	5.3 (1.1)	5.1 (1.2)	0.32 (0.08 to 0.55)**	0.28 (0.08 to 0.47)*	–0.04 (–0.28 to 0.20)
Symptoms	4.2 (0.9)	4.0 (1.1)	4.2 (1.0)	5.2 (1.3)	5.1 (1.1)	4.9 (1.2)	0.39 (0.10 to 0.68)**	0.24 (0.01 to 0.47)*	–0.16 (–0.44 to 0.13)
Activities	5.0 (1.4)	4.8 (1.4)	5.0 (1.3)	5.9 (1.3)	5.6 (1.4)	5.7 (1.3)	0.22 (–0.06 to 0.50)	0.22 (0.01 to 0.44)	0.01 (–0.28 to 0.28)
Emotion	4.0 (1.2)	4.0 (1.4)	4.0 (1.3)	5.4 (1.5)	5.5 (1.3)	5.0 (1.5)	0.43 (0.09 to 0.77)*	0.37 (0.09 to 0.65)**	–0.06 (–0.40 to 0.28)
Environment	3.9 (1.1)	3.8 (1.2)	3.9 (1.2)	5.1 (1.5)	4.9 (1.4)	4.8 (1.5)	0.26 (–0.04 to 0.56)	0.31 (0.06 to 0.57)*	0.05 (–0.24 to 0.35)

*$p < 0.05$, **$p < 0.001$.

TABLE 7 Adjusted mean difference in 12-month AQLQ scores in the DVD, physiotherapy and usual-care treatment arms in the ITT and PP populations

	ITT population			PP population		
	Adjusted mean difference[a] (95% CI)			Adjusted mean difference[a] (95% CI)		
AQLQ domain	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy
Total	0.24 (0.04 to 0.44)*	0.28 (0.11 to 0.44)**	0.04 (–0.16 to 0.24)	0.22 (0.02 to 0.43)*	0.26 (0.10 to 0.43)**	0.04 (–0.17 to 0.25)
Symptoms	0.27 (0.04 to 0.49)*	0.24 (0.05 to 0.42)*	–0.03 (–0.26 to 0.20)	0.25 (0.02 to 0.49)*	0.21 (0.02 to 0.40)*	–0.04 (–0.27 to 0.19)
Activities	0.08 (–0.14 to 0.31)	0.21 (0.04 to 0.41)*	0.13 (–0.10 to 0.36)	0.08 (–0.15 to 0.30)	0.21 (0.02 to 0.39)*	0.13 (–0.10 to 0.36)
Emotion	0.43 (0.16 to 0.71)**	0.38 (0.16 to 0.60)**	–0.06 (–0.33 to 0.22)	0.41 (0.14 to 0.68)**	0.35 (0.13 to 0.58)**	–0.05 (–0.33 to 0.22)
Environment	0.19 (–0.06 to 0.44)	0.32 (0.11 to 0.53)**	0.13 (–0.12 to 0.39)	0.18 (–0.07 to 0.44)	0.32 (0.11 to 0.54)**	0.14 (–0.12 to 0.40)

*$p < 0.05$, **$p < 0.001$.
a Adjusted for prespecified list of covariates.

Between-group Asthma Quality of Life Questionnaire score changes

In the primary efficacy analysis, the between-group comparison of AQLQ scores in the ITT population adjusted for the prespecified covariates, we observed a statistically significant improvement in mean AQLQ score of 0.28 (95% CI 0.11 to 0.44; $p < 0.001$) in the DVD arm compared with the control arm and of 0.24 (95% CI 0.04 to 0.44; $p < 0.05$) in the physiotherapy arm compared with the control arm, confirming the superiority of the two active interventions over usual care. The adjusted mean difference between the DVD arm and the physiotherapy arm was 0.04 (95% CI –0.16 to 0.24), which was not significantly different; the 95% CI was within the prespecified equivalence margin, confirming the equivalence of the two active interventions. Across the AQLQ subdomains, the largest improvements in AQLQ scores for the active treatments compared with usual care were in the emotions subdomain (DVD vs. control: adjusted mean difference 0.38, 95% CI 0.16 to 0.60; $p < 0.001$; physiotherapy vs. control: adjusted mean difference 0.43, 95% CI 0.16 to 0.71; $p < 0.001$); significant improvements were also seen in the symptoms, activities and environment domains in the DVD arm compared with the usual-care arm and in the symptoms domain in the physiotherapy arm compared with the usual-care arm (with non-significant numerical improvements in the physiotherapy arm compared with the usual-care arm for activities and environment). There were no significant differences in subdomain scores between the DVD arm and the physiotherapy arm.

The overall messages were unchanged in the PP population analyses, with superiority of both active treatment arms over usual care and equivalence between the active arms, with the magnitude of the improvements very similar to the magnitude of the improvements in the ITT population. Similarly, in the unadjusted analyses in both the ITT and the PP populations, the overall messages were identical, with superiority of both interventions over usual care and equivalence of the active interventions and only minor differences in the magnitude of the differences between treatment arms.

Time course of Asthma Quality of Life Questionnaire score improvements

The improvements in AQLQ scores in both active arms compared with the control arm were observed at the first post-intervention assessment at 3 months and were maintained or increased over the 12-month study period. In the DVD arm, the improvement in mean total AQLQ score compared with baseline in the ITT population was 0.9 at 3 months, 1.0 at 6 months and 1.1 at 12 months; the equivalent values in the

TABLE 8 Mean AQLQ scores across all time points in the DVD, physiotherapy and usual-care arms in the ITT and PP populations

	Time point, mean (SD) score											
	Baseline			3 months			6 months			12 months		
AQLQ domain	DVD	Physiotherapy	Usual care	DVD	Physiotherapy	Usual care	DVD	Physiotherapy	Usual care	DVD	Physiotherapy	Usual care
ITT population												
n	244	120	246	171	105	226	163	101	217	231	121	241
Total	4.3 (0.9)	4.2 (0.9)	4.3 (0.9)	5.1 (1.2)	5.2 (1.0)	4.9 (1.1)	5.3 (1.3)	5.3 (1.0)	4.9 (1.2)	5.4 (1.1)	5.3 (1.1)	5.1 (1.2)
Symptoms	4.2 (1.0)	4.0 (1.1)	4.2 (1.1)	5.1 (1.2)	5.1 (1.1)	4.7 (1.2)	5.2 (1.2)	5.3 (1.1)	4.7 (1.3)	5.2 (1.3)	5.2 (1.1)	4.9 (1.2)
Activities	5.0 (1.4)	4.8 (1.5)	5.0 (1.3)	5.7 (1.4)	5.6 (1.3)	5.5 (1.4)	5.7 (1.4)	5.7 (1.2)	5.4 (1.4)	5.9 (1.3)	5.7 (1.4)	5.7 (1.3)
Emotion	4.0 (1.3)	4.0 (1.4)	3.9 (1.4)	5.0 (1.4)	5.1 (1.4)	4.8 (1.6)	5.2 (1.4)	5.3 (1.4)	4.8 (1.5)	5.4 (1.5)	5.5 (1.3)	5.0 (1.6)
Environment	4.0 (1.1)	3.8 (1.2)	3.9 (1.2)	4.8 (1.4)	4.8 (1.4)	4.5 (1.3)	4.9 (1.4)	5.0 (1.2)	4.5 (1.4)	5.1 (1.5)	5.0 (1.3)	4.8 (1.5)
PP population												
n	215	110	231	154	94	204	148	92	197	215	110	231
Total	4.3 (0.9)	4.2 (0.9)	4.3 (0.9)	5.2 (1.1)	5.2 (1.0)	4.9 (1.1)	5.3 (1.2)	5.3 (1.0)	4.9 (1.2)	5.4 (1.2)	5.3 (1.0)	5.1 (1.2)
Symptoms	4.2 (0.9)	4.0 (1.1)	4.2 (1.0)	5.1 (1.2)	5.1 (1.1)	4.7 (1.2)	5.1 (1.2)	5.3 (1.1)	4.7 (1.3)	5.2 (1.3)	5.1 (1.1)	4.9 (1.2)
Activities	5.0 (1.4)	4.8 (1.4)	5.0 (1.3)	5.7 (1.3)	5.6 (1.2)	5.4 (1.3)	5.7 (1.4)	5.7 (1.2)	5.4 (1.4)	5.9 (1.3)	5.6 (1.4)	5.7 (1.3)
Emotion	4.0 (1.2)	4.0 (1.4)	3.9 (1.3)	5.0 (1.4)	5.2 (1.4)	4.7 (1.5)	5.2 (1.4)	5.4 (1.3)	4.8 (1.5)	5.4 (1.5)	5.5 (1.3)	5.0 (1.5)
Environment	3.9 (1.1)	3.8 (1.2)	3.9 (1.1)	4.8 (1.4)	4.8 (1.4)	4.5 (1.3)	4.9 (1.4)	5.0 (1.2)	4.5 (1.4)	5.1 (1.5)	4.9 (1.4)	4.8 (1.5)

physiotherapy arm were 1.0, 1.1 and 1.1, respectively, and in the control arm were 0.6, 0.6 and 0.8 respectively. Similar patterns of change were seen in the PP population and for the subdomain scores in both the ITT and the PP populations.

Number needed to treat to achieve a clinically important improvement in the primary outcome measure, Asthma Quality of Life Questionnaire score

The number needed to treat (NNT) was calculated using the formula recommended by Guyatt *et al.*[32] (Juniper and Guyatt produced the AQLQ[24] and ACQ[25] tools). This analysis is based on an individual patient assessment of the proportions in each treatment arm showing a clinically significant improvement (≥ 0.5), the proportions showing unchanged scores (–0.49 to 0.49) and the proportions with a clinically significant deterioration (≤ –0.5) (see *Appendix 5*).

We found that, in the ITT population, 62% of participants in the DVD group reported a clinically significant improvement compared with 64% in the physiotherapy group and 56% in the control group (*Table 9*). The corresponding figures for deterioration were 5% in the DVD group, 4% in the physiotherapy group and 9% in the control group. The proportions in the PP population were slightly higher (see *Table 9*), with 74% of the DVD group, 76% of the physiotherapy group and 62% of the control group showing an improvement in QoL and 6% of the DVD group, 5% of the physiotherapy group and 10% of the control group showing a deterioration in QoL.

In between-group comparisons, these figures equated to a NNT for one patient to have a clinically relevant improvement in QoL in the ITT population of eight for the DVD arm compared with the usual-care arm (*Table 10*), seven for the physiotherapy arm compared with the usual-care arm (*Table 11*) and 41 for the physiotherapy arm compared with the DVD arm (*Table 12*). In the PP population the corresponding NNTs were eight, seven and 56 (*Tables 13–15*).

TABLE 9 Proportions of participants by margin of change in AQLQ score from baseline to 12 months in the DVD, physiotherapy and usual-care arms in the ITT and PP populations

	Treatment arm, *n* (%)			
Change in AQLQ score	DVD	Physiotherapy	Usual care	Total, *n* (%)
ITT population				
n	261	132	262	655
Improved	161 (61.7)	85 (64.4)	146 (55.7)	392 (59.8)
Stayed the same	47 (18.0)	24 (18.2)	71 (27.1)	142 (21.7)
Deteriorated	14 (5.4)	5 (3.8)	24 (9.2)	43 (6.6)
Could not be calculated	39 (14.9)	18 (13.6)	21 (8.0)	78 (11.9)
Total	261 (100.0)	132 (100.0)	262 (100.0)	655 (100.0)
PP population				
n	215	110	231	556
Improved	159 (74.0)	83 (75.5)	142 (61.5)	384 (69.1)
Stayed the same	43 (20.0)	22 (20.0)	67 (29.0)	132 (23.7)
Deteriorated	13 (6.0)	5 (4.5)	22 (9.5)	40 (7.2)
Total	215 (100.0)	110 (100.0)	231 (100.0)	556 (100.0)

TABLE 10 Between-group comparisons in the ITT population: DVD vs. usual care

	DVD		
Usual care	Improved (0.725)	Stayed the same (0.212)	Deteriorated (0.063)
Improved (0.606)	0.44	0.13	0.04
Stayed the same (0.295)	0.21	0.06	0.02
Deteriorated (0.010)	0.07	0.02	0.01
NNT for DVD vs. usual care[a]	8.2		

a The NNT for one participant to benefit from breathing retraining is calculated by adding up the values for those who improved, subtracting the values for those who deteriorated and dividing 1 by the result.

TABLE 11 Between-group comparisons in the ITT population: physiotherapy vs. usual care

	Physiotherapy		
Usual care	Improved (0.746)	Stayed the same (0.211)	Deteriorated (0.044)
Improved (0.606)	0.45	0.13	0.03
Stayed the same (0.295)	0.22	0.06	0.01
Deteriorated (0.010)	0.07	0.02	0.00
NNT for physiotherapy vs. usual care[a]	6.8		

a The NNT for one participant to benefit from breathing retraining is calculated by adding up the values for those who improved, subtracting the values for those who deteriorated and dividing 1 by the result.

TABLE 12 Between-group comparisons in the ITT population: physiotherapy vs. DVD

	DVD		
Physiotherapy	Improved (0.725)	Stayed the same (0.212)	Deteriorated (0.063)
Improved (0.746)	0.54	0.16	0.05
Stayed the same (0.211)	0.15	0.04	0.01
Deteriorated (0.044)	0.03	0.01	0.00
NNT for physiotherapy vs. DVD[a]	41.0		

a The NNT for one participant to benefit from breathing retraining is calculated by adding up the values for those who improved, subtracting the values for those who deteriorated and dividing 1 by the result.

TABLE 13 Between-group comparisons in the PP population: DVD vs. usual care

	DVD		
Usual care	Improved (0.725)	Stayed the same (0.212)	Deteriorated (0.063)
Improved (0.614)	0.45	0.12	0.04
Stayed the same (0.290)	0.21	0.06	0.02
Deteriorated (0.010)	0.07	0.02	0.01
NNT for DVD vs. usual care[a]	7.92		

a The NNT for one participant to benefit from breathing retraining is calculated by adding up the values for those who improved, subtracting the values for those who deteriorated and dividing 1 by the result.

TABLE 14 Between-group comparisons in the PP population: physiotherapy vs. usual care[a]

	Physiotherapy		
Usual care	Improved (0.755)	Stayed the same (0.2)	Deteriorated (0.045)
Improved (0.614)	0.46	0.12	0.03
Stayed the same (0.290)	0.22	0.06	0.01
Deteriorated (0.010)	0.07	0.02	0.00
NNT for physiotherapy vs. usual care[a]	6.86		

a The NNT for one participant to benefit from breathing retraining is calculated by adding up the values for those who improved, subtracting the values for those who deteriorated and dividing 1 by the result.

TABLE 15 Between-group comparisons in the PP population: physiotherapy vs. DVD[a]

	DVD		
Physiotherapy	Improved (0.725)	Stayed the same (0.212)	Deteriorated (0.063)
Improved (0.755)	0.56	0.15	0.05
Stayed the same (0.2)	0.15	0.04	0.01
Deteriorated (0.045)	0.03	0.01	0.00
NNT for physiotherapy vs. DVD[a]	55.52		

a The NNT for one participant to benefit from breathing retraining is calculated by adding up the values for those who improved, subtracting the values for those who deteriorated and dividing 1 by the result.

Prespecified sensitivity analysis on the primary outcome

As per the prespecified SAP, we carried out a sensitivity analysis on the primary outcome data, the change in AQLQ scores between baseline and 12 months adjusted for the prespecified covariates. In this analysis we included all randomised patients regardless of whether baseline or follow-up AQLQ data were present and we used the following rules (based on recommendations from Juniper) to assign values to missing data:

1. For missing baseline AQLQ scores, the following rules were adopted. Values for each AQLQ subdomain (symptoms, emotions, activities, environment) were calculated provided at least two-thirds of the items were scored, otherwise the domain value was set to missing. If any domain score was missing, the overall AQLQ score was set to missing and step 2 was followed.
2. Following step 1, any remaining missing baseline AQLQ scores were replaced by their cohort mean (as specified in the SAP).
3. For missing 12-month AQLQ scores, the method of LOCF was applied. If the 12-month score was missing, the 6-month score was used. If both the 12-month and 6-month scores were missing, the 3-month score was used to replace the 12-month score. If the 3-month, 6-month and 12-month scores were missing, that is, no follow-up information was available, then it was assumed that the patient returned to his or her baseline AQLQ score. Hence, the baseline and 12-month scores were the same.

Table 16 shows the baseline and 12-month unadjusted scores and the unadjusted mean differences in the three treatment arms in the ITT and PP populations, and *Table 17* shows the adjusted mean difference in 12-month AQLQ scores in the three treatment arms in the ITT and PP populations. This sensitivity analysis provides a similar message to the primary analyses: we see that there are significant improvements in both of the active arms (DVD and physiotherapy) above usual care in both the ITT and PP populations, although predictably of slightly lower magnitude (as we assume 'no change' in cases with missing data) than in the main analysis. We continue to show equivalence between the two active arms.

TABLE 16 Baseline to 12 month unadjusted change in AQLQ scores in the DVD, physiotherapy and usual-care arms in the ITT population[a]

	Time point, mean (SD) score								
	Baseline			12 months			Unadjusted mean difference (95% CI)		
AQLQ domain	DVD	Physiotherapy	Usual care	DVD	Physiotherapy	Usual care	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy
ITT population									
n	261	132	262	261	132	262			
Total	4.3 (0.9)	4.2 (0.9)	4.3 (0.9)	5.3 (1.1)	5.3 (1.1)	5.1 (1.2)	0.26 (0.05 to 0.48)*	0.17 (–0.01 to 0.35)	–0.09 (–0.31 to 0.12)
Symptoms	4.2 (1.0)	4.1 (1.1)	4.2 (1.0)	5.1 (1.3)	5.1 (1.2)	4.9 (1.2)	0.37 (0.10 to 0.63)**	0.17 (–0.04 to 0.38)	–0.19 (–0.45 to 0.06)
Activities	5.0 (1.3)	4.8 (1.4)	5.0 (1.3)	5.8 (1.4)	5.6 (1.4)	5.6 (1.4)	0.16 (–0.09 to 0.42)	0.11 (–0.09 to 0.32)*	–0.05 (–0.30 to 0.20)
Emotion	4.0 (1.3)	4.1 (1.3)	4.0 (1.3)	5.2 (1.6)	5.4 (1.4)	5.0 (1.6)	0.31 (0.001 to 0.62)*	0.25 (–0.01 to 0.50)	–0.06 (–0.37 to 0.24)
Environment	4.0 (1.1)	3.8 (1.2)	3.9 (1.1)	5.0 (1.5)	5.0 (1.4)	4.8 (1.5)	0.21 (–0.05 to 0.48)	0.13 (–0.10 to 0.37)	–0.08 (–0.36 to 0.20)
PP population									
n	261	123	262	261	123	262			
Total	4.3 (0.9)	4.2 (0.9)	4.3 (0.9)	5.3 (1.2)	5.3 (1.1)	5.1 (1.2)	0.30 (0.08 to 0.52)*	0.17 (–0.01 to 0.35)	–0.13 (–0.35 to 0.09)
Symptoms	4.2 (1.0)	4.0 (1.1)	4.2 (1.0)	5.1 (1.3)	5.1 (1.2)	4.9 (1.2)	0.40 (0.12 to 0.67)*	0.17 (–0.04 to 0.38)	–0.22 (–0.49 to 0.04)
Activities	5.0 (1.3)	4.8 (1.4)	5.0 (1.3)	5.8 (1.4)	5.6 (1.4)	5.6 (1.4)	0.19 (–0.08 to 0.45)	0.11 (–0.09 to 0.32)	–0.08 (–0.33 to 0.18)
Emotion	4.0 (1.3)	4.0 (1.3)	4.0 (1.3)	5.2 (1.6)	5.4 (1.4)	5.0 (1.6)	0.36 (0.04 to 0.68)*	0.25 (–0.01 to 0.50)	–0.11 (–0.43 to 0.20)
Environment	4.0 (1.1)	3.8 (1.2)	3.9 (1.1)	5.0 (1.5)	5.0 (1.4)	4.8 (1.5)	0.27 (–0.005 to 0.53)	0.13 (–0.10 to 0.37)	–0.13 (–0.42 to 0.15)

*$p < 0.05$, **$p < 0.001$.

a Using prespecified sensitivity analysis, as described in accompanying text.

TABLE 17 Adjusted mean difference in 12-month AQLQ scores in the DVD, physiotherapy and usual-care treatment arms in the ITT and PP populations[a]

	ITT population			PP population		
	Adjusted mean difference[b] (95% CI)			Adjusted mean difference[b] (95% CI)		
AQLQ domain	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy
Total	0.21 (0.02 to 0.40)*	0.17 (0.02 to 0.33)*	–0.04 (–0.23 to 0.15)	0.25 (0.06 to 0.44)*	0.17 (0.01 to 0.33)*	–0.08 (–0.27 to 0.12)
Symptoms	0.26 (0.04 to 0.47)*	0.16 (–0.02 to 0.34)	–0.09 (–0.31 to 0.12)	0.29 (0.07 to 0.51)*	0.16 (–0.02 to 0.34)	–0.13 (–0.35 to 0.09)
Activities	0.06 (–0.14 to 0.27)	0.13 (–0.05 to 0.30)	0.06 (–0.15 to 0.27)	0.10 (–0.11 to 0.31)	0.12 (–0.05 to 0.30)	0.02 (–0.19 to 0.24)
Emotion	0.32 (0.06 to 0.58)*	0.23 (0.02 to 0.45)*	–0.09 (–0.34 to 0.17)	0.36 (0.10 to 0.62)*	0.23 (0.02 to 0.44)*	–0.13 (–0.39 to 0.14)
Environment	0.16 (–0.07 to 0.40)	0.18 (–0.02 to 0.38)	0.01 (–0.23 to 0.25)	–0.18 (–0.46 to 0.9)	0.22 (–0.03 to 0.46)	–0.04 (–0.29 to 0.21)

*$p < 0.05$.
a Using prespecified sensitivity analysis, as described in accompanying text.
b Adjusted for prespecified list of covariates.

Secondary outcome measures

Physiological measures

Physiological outcome measures studied related-to-lung function (FEV_1, FEV_1% predicted, FVC, FEV_1/FVC ratio, PEFR) and airway inflammation (FeNO). Measures were taken at baseline and 12 months. The primary analysis (*Table 18*) assessed change in physiological parameters between baseline and 12 months in the ITT population, adjusted for the prespecified covariates; secondary analyses assessed these parameters in the unadjusted ITT population (*Table 19*) and the adjusted and unadjusted PP populations (see *Tables 14* and *15*).

TABLE 18 Adjusted change in physiological parameters at 12 months in the DVD, physiotherapy and usual-care treatment arms in the ITT and PP populations

	ITT population			PP population		
	Adjusted mean difference[a] (95% CI)			Adjusted mean difference[a] (95% CI)		
Parameters	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy
FEV_1 (l)	–0.04 (–0.11 to 0.04)	–0.001 (–0.07 to 0.07)	0.03 (–0.05 to 0.12)	0.02 (–0.06 to 0.11)	–0.01 (–0.08 to 0.07)	–0.03 (–0.12 to 0.06)
FVC (l)	–0.04 (–0.16 to 0.08)	–0.03 (–0.14 to 0.07)	0.01 (–0.12 to 0.13)	0.03 (–0.09 to 0.16)	0.02 (–0.09 to 0.13)	–0.01 (–0.14 to 0.12)
FEV_1-to-FVC ratio	–0.01 (–0.02 to 0.01)	0.004 (–0.01 to 0.02)	0.01 (–0.01 to 0.03)	0.01 (–0.02 to 0.02)	–0.003 (–0.02 to 0.01)	–0.004 (–0.03 to 0.02)
FEV_1% predicted	0.44 (–3.23 to 4.12)	0.53 (–2.75 to 3.81)	0.09 (–3.81 to 3.99)	–1.49 (–5.33 to 2.36)	–0.98 (–4.35 to 2.39)	0.51 (–3.55 to 4.57)
PEFR (l/second)	–4.79 (–22.35 to 12.77)	–1.99 (–17.83 to 13.85)	2.80 (–15.94 to 21.54)	3.19 (–15.41 to 21.80)	2.91 (–13.66 to 19.48)	–0.29 (–20.10 to 19.53)
FeNO[b] (p.p.b.)	1.05 (0.95 to 1.23)	1.13 (0.98 to 1.29)	1.07 (0.91 to 1.25)	1.05 (0.89 to 1.23)	1.14 (0.98 to 1.31)	1.08 (0.92 to 1.28)

p.p.b., parts per billion.
a Adjusted for prespecified list of covariates.
b Geometric mean difference.

TABLE 19 Unadjusted change in physiological parameters from baseline to 12 months in the DVD, physiotherapy and usual-care treatment arms in the ITT and PP populations

	Time point								
	Baseline			12 months			Unadjusted mean difference (95% CI)		
Parameters	DVD	Physiotherapy	Usual care	DVD	Physiotherapy	Usual care	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy
ITT population									
n	261	132	262	143	92	189			
FEV_1 (l), mean (SD)	2.6 (0.8)	2.5 (0.7)	2.6 (0.8)	2.6 (0.8)	2.4 (0.7)	2.5 (0.7)	0.01 (–0.06 to 0.09)	–0.02 (–0.08 to 0.04)	–0.03 (–0.09 to 0.02)
FVC (l), mean (SD)	3.5 (0.9)	3.3 (0.9)	3.4 (0.9)	3.6 (1.0)	3.2 (0.8)	3.4 (0.9)	0.01 (–0.11 to 0.13)	–0.01 (–0.09 to 0.09)	–0.01 (–0.10 to 0.09)
FEV_1/FVC ratio, mean (SD)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.7 (0.1)	0.8 (0.1)	0.003 (–0.02 to 0.02)	–0.02 (–0.02 to 0.02)	–0.005 (–0.02 to 0.01)
FEV_1% predicted, mean (SD)	90.5 (18.8)	88.8 (18.1)	91.9 (21.6)	90.5 (19.2)	89.5 (19.5)	91.9 (17.4)	–2.05 (–5.78 to 1.68)	–2.02 (–4.9 to 0.89)	0.03 (–2.89 to 2.96)
PEFR (l/second), mean (SD)	425.5 (115.7)	414.9 (110.0)	423.4 (120.7)	422.7 (122.3)	400.1 (114.7)	415.1 (117.2)	4.49 (–11.15 to 20.13)	2.32 (–11.36 to 15.99)	–2.17 (–15.54 to 11.19)
FeNO (p.p.b.), median (IQR)	21 (14–35)	23 (15–33)	23 (14–34)	20 (13–33)	21 (13–32)	20 (13–31)	Unadjusted median difference, *p*-value:		
							$Z = -1.09$, $r = -0.07$;[a] $p = 0.28$	$Z = -2.412$, $r = -0.14$;[a] $p = 0.02$	$Z = -0.941$, $r = -0.06$;[a] $p = 0.35$
PP population									
n	215	110	231	134	83	180			
FEV_1 (l), mean (SD)	2.6 (0.8)	2.4 (0.7)	2.6 (0.8)	2.6 (0.8)	2.4 (0.7)	2.5 (0.7)	–0.003 (–0.08 to 0.08)	–0.03 (–0.001 to 0.07)	–0.02 (–0.08 to 0.03)
FVC (l), mean (SD)	3.5 (0.9)	3.2 (0.8)	3.4 (0.9)	3.5 (1.0)	3.3 (0.8)	3.4 (0.9)	–0.004 (–0.13 to 0.13)	–0.02 (–0.13 to 0.09)	–0.01 (–0.1 to 0.09)
FEV_1/FVC ratio, mean (SD)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.7 (0.1)	0.8 (0.1)	–0.0004 (–0.02 to 0.02)	–0.001 (–0.02 to 0.02)	–0.001 (–0.02 to 0.02)
FEV_1% predicted, mean (SD)	90.3 (19.3)	87.6 (17.9)	92.2 (21.8)	90.5 (16.6)	89.8 (18.9)	91.6 (17.3)	–3.29 (–7.16 to 0.57)	–2.39 (–5.45 to 0.66)	0.90 (–1.99 to 3.79)
PEFR (l/second), mean (SD)	422.5 (118.8)	410.5 (108.1)	421.9 (120.4)	419.6 (121.4)	401.3 (110.2)	413.3 (118.0)	3.0 (–13.56 to 19.57)	3.3 (–11.05 to 17.71)	0.33 (–13.67 to 14.33)
FeNO (p.p.b.), median (IQR)	21 (15–35)	22 (15–34)	22.5 (14–34.5)	19 (13–33)	21 (13–32)	20 (13–31)	Unadjusted median difference, *p*-value:		
							$Z = -0.85$, $r = -0.05$;[a] $p = 0.40$	$Z = -2.12$, $r = -0.13$;[a] $p = 0.03$	$Z = -0.91$, $r = -0.06$;[a] $p = 0.36$

p.p.b., parts per billion.
a Cohen's effect size.

In the primary analysis we observed no significant between-group changes in our measures of airway physiology or inflammation, indicating that the interventions did not change obstruction or inflammation in the airways and so were not disease modifying. The within-group changes from baseline to 12 months were small and non-significant.

We observed no significant changes in the within-group mean scores (geometric mean for FeNO readings) between baseline and 12 months for any of these parameters. In the unadjusted analyses there was a small but statistically significant difference in the change in median FeNO score from baseline to 12 months in the ITT population in the DVD group (from 21 to 20) compared with the control group (from 23 to 20; $p = 0.03$), but this difference was not seen in the primary (i.e. adjusted for covariates) analysis. None of the lung function parameters changed significantly from baseline in any of the treatment arms in the ITT and PP populations.

These findings suggest that the improvements in QoL seen in our primary outcome measure (AQLQ score) were not mediated by changes in the pathophysiology of asthma; this will be considered in *Chapter 7*.

Patient-reported outcome measures (questionnaires)

We included a number of validated questionnaires as secondary outcome measures: the ACQ (measuring asthma symptoms), the Nijmegen questionnaire (measuring symptoms related to hyperventilation and dysfunctional breathing) and the HADS, with separate domains measuring anxiety and depression. Our main analysis was a comparison of the mean score changes between baseline and 12 months in the ITT population between the study arms, with adjustments for prespecified covariates (*Table 20*). In secondary analyses we compared mean score changes between baseline and 12 months in the PP population between study arms, with adjustments for prespecified covariates (see *Table 16*) and unadjusted changes in questionnaire scores in the ITT population and the PP population (*Table 21*).

We found no significant changes in asthma symptom control, anxiety scores or Nijmegen questionnaire scores in the active intervention groups compared with the control group in either the ITT or the PP population. We did observe a small magnitude but statistically significant improvement in depression scores in the DVD treatment arm compared with the control arm, with a similar magnitude but statistically non-significant difference in the physiotherapy arm compared with the control arm. However, the baseline

TABLE 20 Adjusted questionnaire scores at 12 months in the DVD, physiotherapy and usual-care treatment arms in the ITT and PP populations

	ITT population			PP population		
	Adjusted mean difference[a] (95% CI)			Adjusted mean difference[a] (95% CI)		
Questionnaire	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy
ACQ	–0.06 (–0.23 to 0.13)	–0.09 (–0.25 to 0.06)	–0.04 (–0.23 to 0.15)	–0.04 (–0.22 to 0.15)	–0.05 (–0.21 to 0.11)	–0.01 (–0.20 to 0.19)
HADS						
Anxiety	–0.04 (–0.73 to 0.64)	–0.22 (–0.81 to 0.38)	–0.18 (–0.89 to 0.54)	0.03 (–0.71 to 0.75)	–0.16 (–0.79 to 0.47)	–0.17 (–0.94 to 0.58)
Depression	–0.55 (–1.14 to 0.04)	–0.56 (–1.07 to –0.05)*	–0.01 (–0.63 to 0.60)	–0.58 (–1.19 to 0.04)	–0.56 (–1.10 to –0.03)*	0.02 (–0.62 to 0.66)
Nijmegen questionnaire	1.28 (–0.55 to 3.12)	0.90 (–0.71 to 2.51)	–0.38 (–2.30 to 1.55)	1.41 (–0.50 to 3.32)	0.99 (–0.67 to 2.65)	–0.42 (–2.42 to 1.58)

*$p < 0.05$.
a Adjusted for prespecified list of covariates.

TABLE 21 Unadjusted change in questionnaire scores from baseline to 12 months in the DVD, physiotherapy and usual-care treatment arms in the ITT and PP populations

Questionnaire	Time point: Baseline			Time point: 12 months			Unadjusted mean difference (95% CI)		
	DVD	Physiotherapy	Usual care	DVD	Physiotherapy	Usual care	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy
ITT population									
n	260	132	262	159	96	194			
ACQ, mean (SD)	1.5 (0.9)	1.6 (0.8)	1.5 (0.9)	1.2 (0.9)	1.3 (0.8)	1.2 (0.8)	–0.15 (–0.3 to 0.04)	–0.09 (–0.27 to 0.08)	0.06 (–0.13 to 0.26)
Nijmegen questionnaire, mean (SD)	19.0 (8.8)	18.9 (10.5)	19.4 (9.4)	16.9 (9.4)	17.1 (9.8)	18.3 (9.3)	0.87 (–0.7 to 2.5)	0.8 (–0.5 to 2.2)	–0.03 (–1.6 to 1.5)
HADS									
Anxiety									
Median (IQR)	7 (4–8)	6 (4–9)	6 (4–9)	5 (3–8)	6 (3–8)	6 (3–9)	Unadjusted median difference, *p*-value:		
Minimum, maximum	0, 19	0, 20	0, 20	0, 16	0, 18	0, 18.7	$Z = -0.04$, $r = -0.0021$; $p = 0.96$	$Z = -0.66$, $r = -0.041$; $p = 0.5$	$Z = -0.50$, $r = -0.031$; $p = 0.62$
Depression									
Median (IQR)	3 (1–5)	2 (1–5)	3 (1–5)	2 (1–5)	3 (1–4)	3 (1–5)	Unadjusted median difference, *p*-value:		
Minimum, maximum	0, 17	0, 17	0, 14	0, 13	0, 17	0, 16	$Z = -1.92$, $r = -0.11$;[a] $p = 0.6$	$Z = -2.94$,* $r = -0.161$;[a] $p = 0.03$	$Z = -0.65$, $r = -0.041$;[a] $p = 0.52$
PP population									
n	215	110	231	147	91	193			
ACQ, mean (SD)	1.5 (0.8)	1.6 (0.8)	1.5 (0.9)	1.2 (0.9)	1.3 (0.8)	1.3 (0.8)	0.13 (–0.07 to 0.34)	0.05 (–0.13 to 0.24)	–0.08 (–0.28 to 0.12)
Nijmegen questionnaire, mean (SD)	18.6 (8.7)	18.7 (10.5)	19.6 (9.2)	16.8 (9.5)	17.1 (9.5)	18.7 (9.2)	0.96 (–0.74 to 2.66)	0.81 (–0.61 to 2.22)	–0.15 (–1.77 to 1.47)

continued

TABLE 21 Unadjusted change in questionnaire scores from baseline to 12 months in the DVD, physiotherapy and usual-care treatment arms in the ITT and PP populations (*continued*)

Questionnaire	Time point: Baseline			Time point: 12 months			Unadjusted mean difference (95% CI)		
	DVD	Physiotherapy	Usual care	DVD	Physiotherapy	Usual care	Physiotherapy vs. usual care	DVD vs. usual care	DVD vs. physiotherapy
HADS									
Anxiety									
Median (IQR)	6 (4–8)	6 (4–9)	6 (4–9)	5 (3–9)	6 (3–8)	6 (4–9)	Unadjusted median difference, *p*-value:		
Minimum, maximum	0, 19	0, 18	0, 18	0, 16	0, 18	0, 19	$Z = -0.12$, $r = -0.01$;[a] $p = 0.91$	$Z = -0.37$, $r = -0.02$;[a] $p = 0.7$	$Z = -0.28$, $r = -0.02$;[a] $p = 0.78$
Depression									
Median (IQR)	3 (1–5)	2 (1–5)	3 (1–4)	2 (1–5)	3 (1–5)	3 (1–6)	Unadjusted median difference, *p*-value:		
Minimum, maximum	0, 17	0, 17	0, 14	0, 13	0, 17	0, 16	$Z = -2.07$, $r = -0.001$;[a] $p = 0.04$	$Z = -2.7$, $r = -0.15$;[a] $p = 0.01$	$Z = -0.23$, $r = -0.02$;[a] $p = 0.82$

*$p < 0.05$.
a Cohen's effect size.

depression scores were low and few participants met 'caseness' criteria for depression, with depression scores being lower than anxiety scores in the study population. This suggests that depression was not a significant factor in these patients and that the low magnitude changes in depression scores are unlikely to explain the improvements in QoL observed in the active treatment arms. We did observe within-group changes from baseline of 0.2–0.3 units in the mean ACQ score (with a change of 0.5 signifying a clinically important change for an individual patient), indicating that there were modest improvements in the asthma symptoms experienced in all treatment arms. Similarly, although there were improvements in anxiety and Nijmegen questionnaire scores between baseline and 12 months in each group, there was no significant between-group difference in these parameters, indicating that the active interventions did not significantly improve anxiety or hyperventilation-related symptoms and that the mechanism responsible for the improved disease-specific QoL scores in the active treatment groups was not related to improvements in these factors.

Asthma exacerbations

Asthma exacerbations (attacks) were assessed [using the European Respiratory Society (ERS)/American Thoracic Society (ATS) Task Force on asthma outcomes recommendations for defining an exacerbation[33]] according to prescribed short courses of oral corticosteroids for worsening of asthma by the usual physician, with data obtained from the manual and electronic reviews of the patient medical record at 12 months. In keeping with the mild asthma population recruited, only 12% of the ITT population (13% of the PP population) had one or more asthma attack over the 12-month period (*Table 22*). The percentage of patients in the ITT population randomisation treatment arms (DVD, physiotherapy, control) having one or more asthma attack was 9%, 11% and 15%, respectively, and in the PP population was 10%, 12% and 16% respectively (*Table 23*). There was no statistically significant difference in the crude exacerbation rate between the DVD arm and the physiotherapy arm ($p = 0.6$ in the ITT population, $p = 0.8$ in the PP population; *Table 24*) or between the physiotherapy arm and the control arm ($p = 0.4$ for both populations; *Table 25*). The DVD group narrowly failed to reach a statistically significant reduction in exacerbations compared with the control group, with a *p*-value of 0.06 in the ITT population and 0.12 in the PP population) (*Table 26*).

A negative binomial regression model was constructed to assess the between-group differences in asthma exacerbation frequency in the ITT (*Tables 27–29* and *Figure 2*) and PP (*Figure 3* and see *Appendix 6*) populations, adjusting for differences in exacerbation frequency at baseline and for covariates (age, sex, BTS treatment step and smoking status). In the adjusted analysis for the ITT population, the risk of exacerbations

TABLE 22 Oral corticosteroid courses at 12 months in the DVD, physiotherapy and usual-care treatment arms in the ITT and PP populations

	ITT population, *n* (%)				PP population, *n* (%)			
Oral corticosteroid courses	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	Total (*N* = 655)	DVD (*N* = 215)	Physiotherapy (*N* = 110)	Usual care (*N* = 231)	Total (*N* = 556)
None	237 (90.8)	117 (88.6)	223 (85.1)	577 (88.1)	193 (89.8)	97 (88.2)	195 (84.4)	485 (87.2)
1	17 (6.5)	10 (7.6)	26 (9.9)	53 (8.1)	16 (7.4)	9 (8.2)	26 (11.3)	51 (9.2)
2	2 (0.8)	4 (3.0)	10 (3.8)	16 (2.4)	2 (0.9)	3 (2.7)	8 (3.5)	13 (2.3)
3	2 (0.8)	0 (0.0)	1 (0.4)	3 (0.5)	2 (0.9)	0 (0.0)	1 (0.4)	3 (0.5)
≥ 4	3 (1.1)	1 (0.8)	2 (0.8)	6 (0.9)	2 (0.9)	1 (0.9)	1 (0.4)	4 (0.7)
Total	261 (100.0)	132 (100.0)	262 (100.0)	655 (100.0)	215 (100.0)	110 (100.0)	231 (100.0)	556 (100.0)

TABLE 23 Oral corticosteroid courses at 12 months in the DVD, physiotherapy and usual-care treatment arms in the ITT and PP populations: one or more courses

	ITT population, *n* (%)				PP population, *n* (%)			
Oral corticosteroid courses	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	Total (*N* = 655)	DVD (*N* = 215)	Physiotherapy (*N* = 110)	Usual care (*N* = 231)	Total (*N* = 556)
None	237 (90.8)	117 (88.6)	223 (85.1)	577 (88.1)	193 (89.8)	97 (88.2)	195 (84.4)	485 (87.2)
≥ 1	24 (9.2)	15 (11.4)	39 (14.9)	78 (11.9)	22 (10.2)	13 (11.8)	36 (15.6)	71 (12.8)
Total	261 (100.0)	132 (100.0)	262 (100.0)	655 (100.0)	215 (100.0)	110 (100.0)	231 (100.0)	556 (100.0)

TABLE 24 Comparison of oral corticosteroid courses at 12 months in the ITT and PP populations: DVD vs. physiotherapy treatment arms

	ITT population, *n*			PP population, *n*		
Oral corticosteroid courses	DVD (*N* = 261)	Physiotherapy (*N* = 132)	*p*-value	DVD (*N* = 215)	Physiotherapy (*N* = 110)	*p*-value
None	237	117	0.62	193	97	0.81
≥ 1	24	15		22	13	
Total	261	132		215	110	

TABLE 25 Comparison of oral corticosteroid courses at 12 months in the ITT and PP populations: physiotherapy vs. usual care

	ITT population, *n*			PP population, *n*		
Oral corticosteroid courses	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	*p*-value	Physiotherapy (*N* = 110)	Usual care (*N* = 231)	*p*-value
None	117	223	0.42	97	195	0.45
≥ 1	15	39		13	36	
Total	132	262		110	231	

TABLE 26 Comparison of oral corticosteroid courses at 12 months in the ITT and PP populations: DVD vs. usual care

	ITT population, *n*			PP population, *n*		
Oral corticosteroid courses	DVD (*N* = 261)	Usual care (*N* = 262)	*p*-value	DVD (*N* = 215)	Usual care (*N* = 231)	*p*-value
None	237	223	0.06	193	195	0.12
≥ 1	24	39		22	36	
Total	261	132		215	231	

TABLE 27 Group differences in asthma exacerbations in the 12 months post randomisation in the ITT population

	Treatment arm, *n*			
Oral corticosteroid courses	DVD	Physiotherapy	Usual care	Total, *n*
0	237	117	223	577
1	17	10	26	53
2	2	4	10	16
3	2	0	1	3
4	2	1	1	4
6	1	0	0	1
10	0	0	1	1
Total	261	132	262	655

TABLE 28 Unadjusted analysis of the negative binomial regression for asthma exacerbations in the 12 months post randomisation in the ITT population

Comparison	Unadjusted IRR	95% CI	*p*-value
Physiotherapy vs. usual care	0.69	0.34 to 1.41	0.31
DVD vs. usual care	0.65	0.37 to 1.16	0.15
DVD vs. physiotherapy	0.94	0.45 to 1.96	0.87

TABLE 29 Adjusted analysis of the negative binomial regression for asthma exacerbations in the 12 months post randomisation in the ITT population

Comparison	Adjusted IRR[a]	95% CI	*p*-value
Physiotherapy vs. usual care	0.85	0.36 to 1.98	0.89
DVD vs. usual care	0.68	0.34 to 1.38	0.42
DVD vs. physiotherapy	0.81	0.33 to 1.99	0.84

a As there were only 78 cases with one or more oral corticosteroid courses, only the covariates age, sex, BTS treatment step and smoking status were included in the model.

was lower in the DVD arm than in the usual-care arm [incidence rate ratio (IRR) 0.68), but the 95% CI crossed the line of unity (95% CI 0.34 to 1.38) and so this finding was not statistically significant and could have occurred through chance. The analysis of the physiotherapy arm compared with the usual-care arm produced a similar result, with a (lower magnitude) non-significant reduction in the risk of an asthma attack in the physiotherapy arm (IRR 0.85, 95% CI 0.36 to 1.98). There was also no significant difference in the risk of an exacerbation in the DVD group compared with the physiotherapy group, but the DVD group was favoured (IRR 0.81, 95% CI 0.33 to 1.99). The unadjusted negative binomial regression model produced very similar results, as did the adjusted and unadjusted models in the PP population. Our study was not powered to show an effect on exacerbations and, as the annual exacerbation rate is modest in patients with mild and moderate asthma treated in the community, a larger sample would be needed to show a statistically significant reduction in exacerbations. This will be considered further in *Chapter 7*.

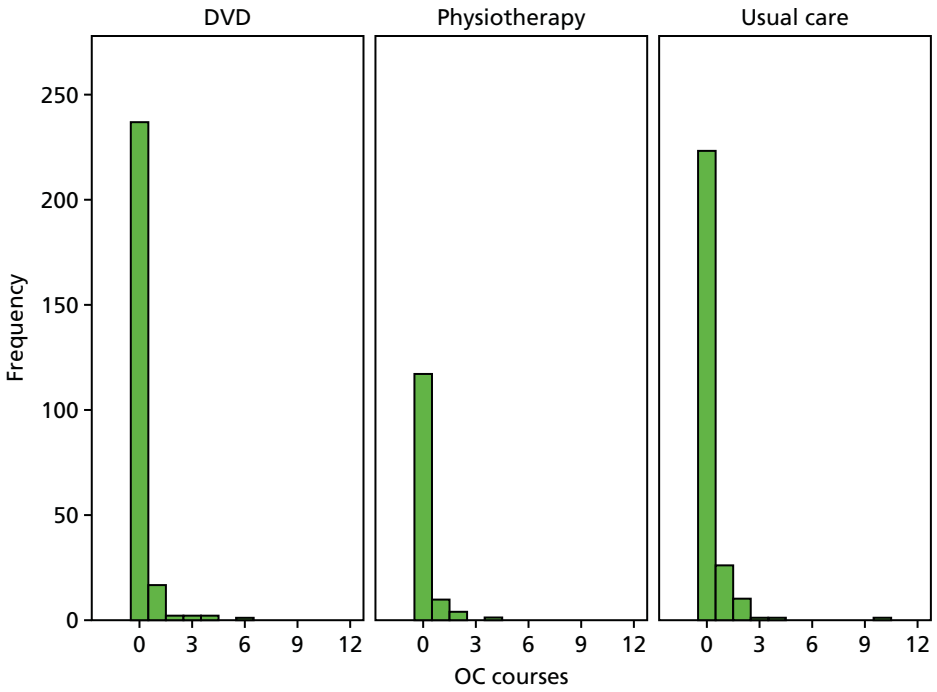

FIGURE 2 Frequency of one or more exacerbations in the 12 months post randomisation by treatment arm in the ITT population. OC, oral corticosteroid.

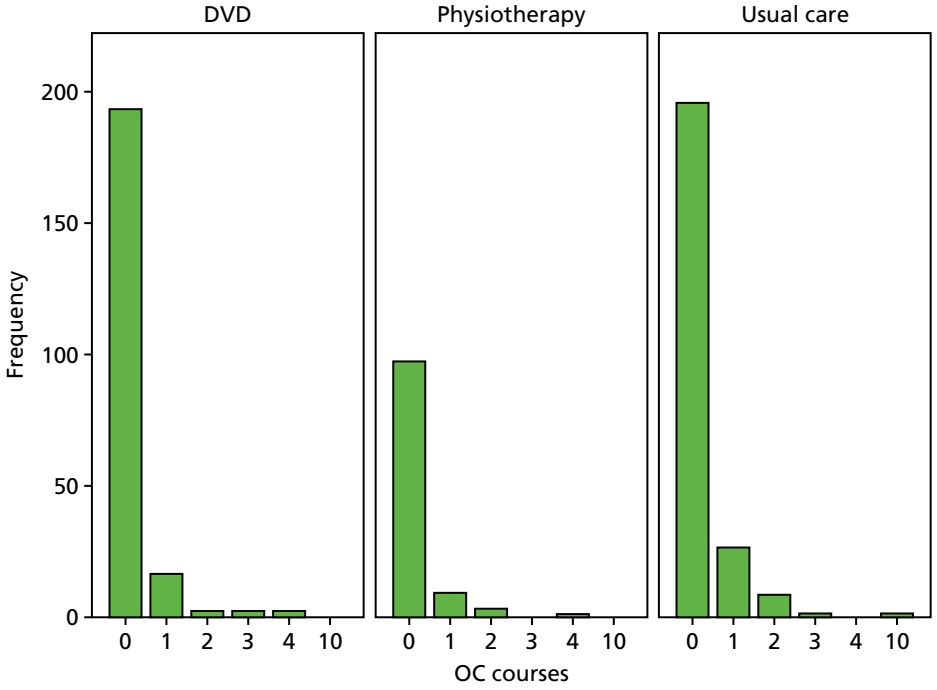

FIGURE 3 Frequency of one or more exacerbations in the 12 months post randomisation by treatment arm in the PP population. OC, oral corticosteroid.

Bronchodilator use

In the 12 months following the baseline assessment, 177 of 261 (67.8%) participants randomised to the DVD arm required one or more prescriptions for rescue bronchodilators compared with 104 of 132 (78.8%) in the physiotherapy arm and 206 of 262 (78.6%) in the control arm. The number of inhalers prescribed over the 12 months post randomisation by treatment arm in the ITT population is shown in *Table 30* and the proportions of participants having each number of inhalers are shown graphically in *Figure 4*. A negative binomial regression model was constructed for the ITT population to estimate the difference in rescue bronchodilator use between arms. In the unadjusted analysis (*Table 31*) there was a non-significant trend for lower bronchodilator use in the DVD arm compared with the usual-care arm (IRR 0.83, 95% CI 0.68 to 1.03; $p = 0.09$) and for the DVD arm compared with the physiotherapy arm (IRR 0.81, 95% CI 0.63 to 1.04; $p = 0.10$), with little difference between physiotherapy arm and the usual-care arm (IRR 1.03, 95% CI 0.81 to 1.33; $p = 0.80$). In the regression model adjusted for covariates (age, sex, BTS treatment step, baseline smoking status, baseline HADS scores and baseline Nijmegen questionnaire score;

TABLE 30 Distribution of rescue inhaler use in the 12 months post randomisation in the ITT population

	Treatment arm, *n*			
Number of rescue inhalers	DVD	Physiotherapy	Usual care	Total, *n*
0	84	28	56	168
1	36	26	61	123
2	39	16	32	87
3	20	18	26	64
4	23	14	24	61
5	17	4	12	33
6	12	6	11	29
7	6	4	5	15
8	6	3	11	20
9	5	2	3	10
10	5	2	6	13
11	2	1	2	5
12	1	3	5	9
13	1	2	0	3
14	2	2	0	4
16	1	0	1	2
17	0	0	1	1
18	0	0	3	3
22	0	0	2	2
26	0	0	1	1
28	1	0	0	1
40	0	1	0	1
Total	261	132	262	655

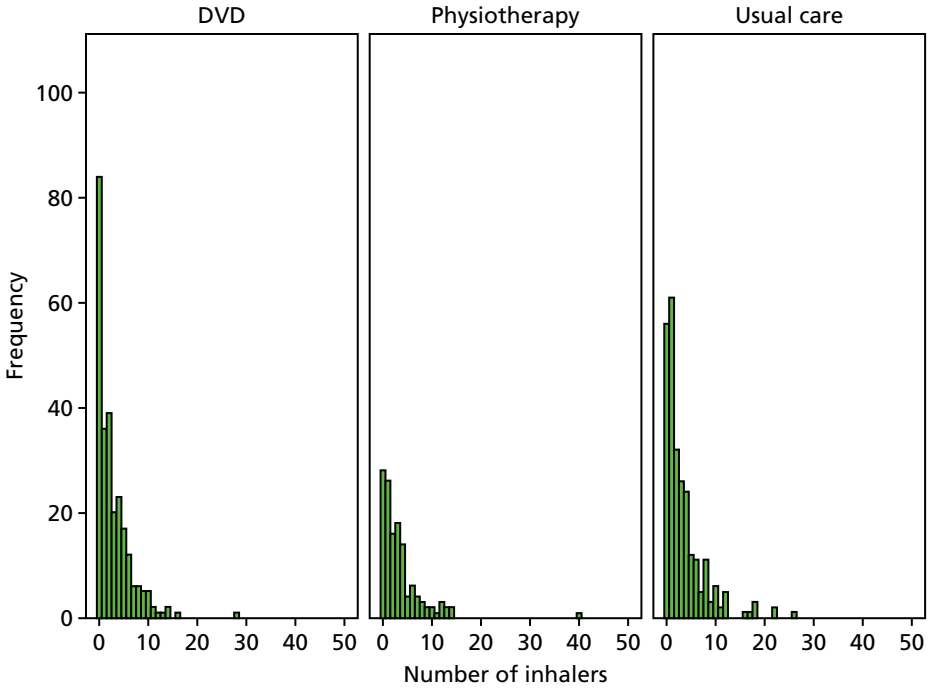

FIGURE 4 Distribution of rescue bronchodilator prescriptions in the 12 months post randomisation by treatment arm in the ITT population.

TABLE 31 Unadjusted analysis of the negative binomial regression for rescue inhaler use in the 12 months after baseline in the ITT population

Comparison	Unadjusted IRR	95% CI	*p*-value
Physiotherapy vs. usual care	1.03	0.81 to 1.33	0.80
DVD vs. usual care	0.83	0.68 to 1.03	0.09
DVD vs. physiotherapy	0.81	0.63 to 1.04	0.10

Table 32), a similar pattern was seen, with the adjusted IRR being 0.91 (95% CI 0.72 to 1.15; $p = 0.61$) for the DVD arm compared with the control arm, 0.88 (95% CI 0.66 to 1.15; $p = 0.50$) for the DVD arm compared with the physiotherapy arm and 1.03 (95% CI 0.79 to 1.37; $p = 0.93$) for the physiotherapy arm compared with the usual-care arm. The same analyses were performed on the PP population, which also found no significant differences in rescue bronchodilator use between randomisation treatment arms in the adjusted or the unadjusted analysis (*Figure 5* and see *Appendix 5*).

TABLE 32 Adjusted analysis of the negative binomial regression for rescue inhaler use in the 12 months after baseline in the ITT population

Comparison	Adjusted IRR[a]	95% CI	*p*-value
Physiotherapy vs. usual care	1.03	0.79 to 1.37	0.93
DVD vs. usual care	0.91	0.72 to 1.15	0.61
DVD vs. physiotherapy	0.88	0.66 to 1.15	0.50

a Adjusted for age, sex, BTS treatment step, baseline smoking status, baseline HADS scores and baseline Nijmegen questionnaire score.

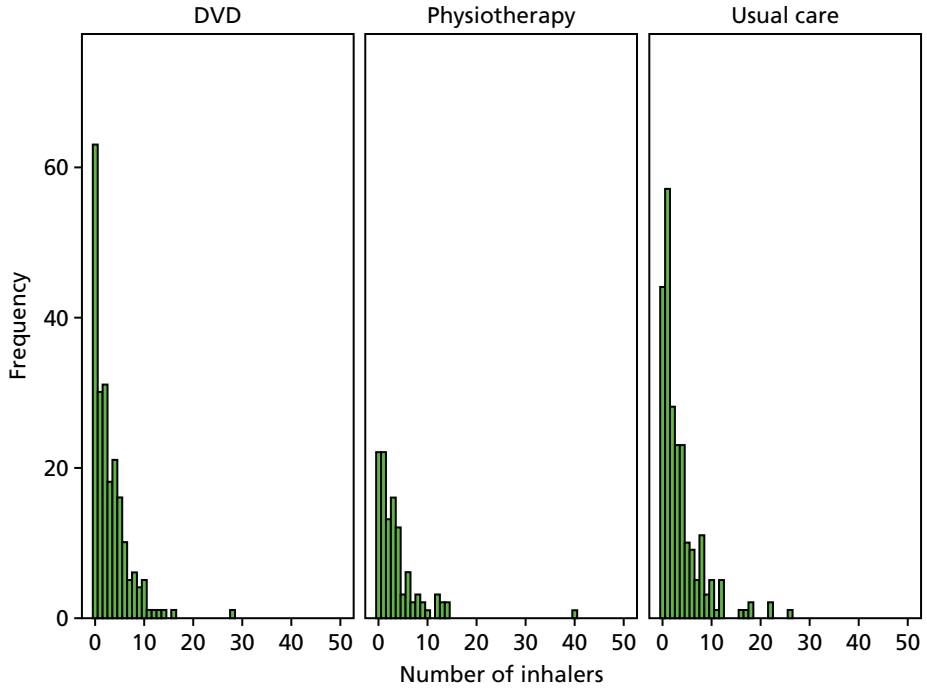

FIGURE 5 Distribution of rescue bronchodilator prescriptions in the 12 months post randomisation by treatment arm in the PP population.

Respiratory-related general practitioner consultations

In the 12 months following randomisation, the number of times that each patient saw a general practitioner (GP) for a respiratory-related reason varied between none and 21 (*Table 33*). In total, 71.2% of the DVD group, 75.1% of the physiotherapy group and 76.7% of the control group had one or more GP consultation. Unadjusted and adjusted negative binomial regression models were constructed to estimate the difference between treatment arms in GP consultation rates. In both adjusted and unadjusted analyses of the ITT population (*Tables 34* and *35*), there were non-significant trends for lower consultation rates in the active arms than in the control arm, with minimal differences between the active arms (DS vs. control: unadjusted IRR 0.87, 95% CI 0.72 to 1.05; adjusted IRR 0.93, 95% CI 0.74 to 1.15; physiotherapy vs. control: unadjusted IRR 0.90, 95% CI 0.72 to 1.12; adjusted IRR 0.94, 95% CI 0.72 to 1.24; DVD vs. physiotherapy: unadjusted IRR 0.97, 95% CI 0.77 to 1.22; adjusted IRR 0.98, 95% CI 0.75 to 1.29). Similar results were found for the PP population (*Tables 36* and *37* and see *Appendix 7*).

It is not possible to determine whether the interventions reduced the need for GP consultations, as the study was underpowered to test this hypothesis, but there is a suggestion that there may have been some reduction in consultation rates (by approximately one-tenth in this sample).

Overall health resource use

The analysis of health resource use is considered in detail in *Chapter 4*.

Overall health resource use was assessed through direct medical costs. The mean NHS cost per patient by arm was aggregated from costs of prescriptions, consultations and hospital admissions. Although there were few hospital admissions (usual-care arm, $n = 8$; physiotherapy arm, $n = 0$; DVD arm, $n = 4$), they were by far the most costly item. The main cost items for each group were asthma-related medications and GP consultations. The mean cost per patient was highest in the control group (£356), with a similar cost in the physiotherapy group (£355) and the lowest cost in the DVD group (£296).

TABLE 33 Numbers of participants in the ITT population having respiratory-related GP consultations in the 12 months post randomisation by treatment group

	Treatment arm, *n* (%)			
Number of GP consultations	DVD	Physiotherapy	Usual care	Total, *n* (%)
0	75 (44.4)	33 (19.5)	61 (36.1)	169 (100.0)
1	103 (39.6)	55 (21.2)	102 (39.2)	260 (100.0)
2	42 (39.6)	24 (22.6)	40 (37.7)	106 (100.0)
3	19 (38.8)	8 (16.3)	22 (44.9)	49 (100.0)
4	8 (32.0)	3 (12.0)	14 (56.0)	25 (100.0)
5	4 (17.4)	6 (26.1)	13 (56.5)	23 (100.0)
6	4 (40.0)	1 (10.0)	5 (50.0)	10 (100.0)
7	2 (50.0)	0 (0.0)	2 (50.0)	4 (100.0)
8	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
9	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
11	1 (33.3)	1 (33.3)	1 (33.3)	3 (100.0)
12	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
15	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)
16	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)
21	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
Total	261 (39.8)	132 (20.2)	262 (40.0)	655 (100.0)

TABLE 34 Unadjusted analysis of the negative binomial regression for respiratory-related GP appointments in the 12 months after baseline in the ITT population

Comparison	Unadjusted IRR	95% CI	*p*-value
Physiotherapy vs. usual care	0.90	0.72 to 1.12	0.35
DVD vs. usual care	0.87	0.72 to 1.05	0.14
DVD vs. physiotherapy	0.97	0.77 to 1.22	0.78

TABLE 35 Adjusted analysis of the negative binomial regression for respiratory-related GP appointments in the 12 months after baseline in the ITT population

Comparison	Adjusted IRR[a]	95% CI	*p*-value
Physiotherapy vs. usual care	0.94	0.72 to 1.24	0.87
DVD vs. usual care	0.93	0.74 to 1.15	0.69
DVD vs. physiotherapy	0.98	0.75 to 1.29	0.95

a Adjusted for age, sex, BTS treatment step, baseline smoking status, baseline HADS scores and baseline Nijmegen questionnaire score.

TABLE 36 Unadjusted analysis of the negative binomial regression for respiratory-related GP appointments in the 12 months after baseline in the PP population

Comparison	Unadjusted IRR	95% CI	*p*-value
Physiotherapy vs. usual care	0.90	0.71 to 1.14	0.37
DVD vs. usual care	0.85	0.71 to 1.04	0.11
DVD vs. physiotherapy	0.95	0.75 to 1.21	0.68

TABLE 37 Adjusted analysis of the negative binomial regression for respiratory-related GP appointments in the 12 months after baseline in the PP population

Comparison	Adjusted IRR[a]	95% CI	*p*-value
Physiotherapy vs. usual care	0.93	0.71 to 1.22	0.84
DVD vs. usual care	0.88	0.69 to 1.10	0.35
DVD vs. physiotherapy	0.96	0.72 to 1.24	0.84

a Adjusted for age, sex, BTS treatment step, baseline smoking status, baseline HADS scores and baseline Nijmegen questionnaire score.

Patient engagement with the intervention in the active treatment arms

Patient engagement was assessed as part of our prespecified analysis plan; the data are presented in *Tables 38* and *39*. Engagement was good in the physiotherapy arm, with 95% of participants attending at least one of the three scheduled sessions and 93% attending all three. Patient experience of the different components of the intervention was generally favourable and the majority of patients spent a considerable amount of time practising the various techniques taught, with over half spending half a day or more practising each technique. The main factor hindering the practising of techniques was practical problems, for example finding time.

Similarly, engagement was good in the DVD arm, although the overall engagement scores for the different components of the intervention were generally slightly lower than those in the physiotherapy arm and the time spent practising the various techniques was lower. Practical problems were again the main hindering factor, although some participants reported uncertainty or doubts over the instructions provided.

These findings are discussed further in *Chapter 6*.

As a prespecified analysis, we compared changes in the primary outcome (AQLQ) between the physiotherapy arm and the DVD arm, including the 'amount of practice' as a covariate and excluding participants who did not engage with the breathing retraining at 3 months in the physiotherapy arm, with data presented for the 3-month evaluation and the 12-month evaluation (see *Appendix 8*). This was carried out to assess whether engagement with the exercises was different between the active arms and whether this could be reflected in differences in primary outcome scores, as the physiotherapists suspected that some patients failed to engage and so had poor outcomes from the face-to-face training programmes, whereas those who did engage generally did well.

Compared with the primary efficacy analysis, this analysis including engagement and time spent practising increased the magnitude of the AQLQ changes in the physiotherapy arm at 3 months, but did not result in significant differences between the DVD arm and the physiotherapy arm, which continued to reach the equivalence margin at the 12-month evaluation, and did not change the message emerging from the study. These findings are discussed further in *Chapter 6*.

TABLE 38 Measures of treatment engagement: physiotherapy arm

Measure	Physiotherapy arm (*N* = 132)
Number of sessions attended, *n* (%)	
n	132
None	6 (4.5)
At least one	126 (95.5)
At least two	123 (93.2)
At least three	123 (93.2)
Treatment experience score[a]	
n	104
Stomach breathing, median (IQR); minimum, maximum	8 (6–9); 3, 10
Nose breathing, median (IQR); minimum, maximum	8 (6–9); 3, 10
Slow breathing, median (IQR); minimum, maximum	7 (5–8); 1, 10
Controlled breath holding, median (IQR); minimum, maximum	5 (4–7); 1, 10
Relaxation training, median (IQR); minimum, maximum	8 (6–9); 1, 10
Total time spent on each breathing technique,[b] *n* (%)[c]	
Stomach breathing	
Weeks – did not use	1 (1.0)
1–5 weeks	20 (19.0)
≥ 6 weeks	79 (75.2)
Hours – did not use	1 (1.0)
Up to 1 hour	44 (41.9)
Up to half a day or more	54 (51.4)
Nose breathing	
Weeks – did not use	1 (1.0)
1–5 weeks	20 (19.0)
≥ 6 weeks	80 (76.2)
Hours – did not use	3 (2.9)
Up to 1 hour	33 (31.4)
Up to half a day or more	65 (61.9)
Slow breathing	
Weeks – did not use	2 (1.9)
1–5 weeks	32 (30.5)
≥ 6 weeks	67 (63.8)
Minutes – did not use	3 (2.9)
Up to 10 minutes	54 (51.4)
> 10 minutes	44 (41.9)

TABLE 38 Measures of treatment engagement: physiotherapy arm (*continued*)

Measure	Physiotherapy arm (*N* = 132)
Controlled breath holding	
Weeks – did not use	10 (9.5)
1–5 weeks	38 (36.2)
≥ 6 weeks	53 (50.5)
Minutes – did not use	12 (11.4)
Up to 5 minutes	64 (61.0)
> 5 minutes	25 (23.8)
Relaxation training	
Weeks – did not use	13 (12.4)
1–5 weeks	38 (36.2)
≥ 6 weeks	50 (47.6)
Minutes – did not use	15 (14.3)
Up to 10 minutes	69 (65.7)
> 10 minutes	17 (16.2)
Treatment engagement score	
n	104
Problems due to symptoms, median (IQR); minimum, maximum	0 (0–0); 0, 12
Problems due to uncertainty about the therapy, median (IQR); minimum, maximum	0 (0–0); 0, 12
Problems due to doubts about the therapy, median (IQR); minimum, maximum	0 (0–0); 0, 12
Practical problems, median (IQR); minimum, maximum	4.5 (1–9); 0, 20
Problems due to lack of support, median (IQR); minimum, maximum	0 (0–0); 0, 12

a Based on different types of breathing retraining.
b Weeks, hours and minutes per day.
c Denominator is those with treatment adherence questionnaire available at 3 months (*n* = 105).

Adverse events

Adverse events were collected for all randomised patients by patients and study centre principal investigators (PIs) on adverse event report forms and by manual and electronic review of medical records at 12 months. Adverse events were categorised by PIs according to the classification scheme provided in *Appendix 9*.

Serious adverse events

The serious adverse event rate was low, with no study-related serious adverse events and an overall rate of 5%. The highest serious adverse event rate was in the control group (7.6%), with lower rates in the DVD group (4.2%) and the physiotherapy group (3%) (*Table 40*). A full list of all serious adverse events reported is provided in *Appendix 10*.

Other adverse events

In total, 744 adverse events were reported from 272 patients (41.5% of the randomised population), with quantification by category and randomisation group provided in *Table 41*. Of the adverse events, 47% occurred in the control arm, 36% occurred in the DVD arm and 17% occurred in the physiotherapy arm (note that there was a 2 : 1 : 2 randomisation schedule between the DVD, physiotherapy and control arms and so the adverse event rate was very similar between the DVD arm and the physiotherapy arm).

TABLE 39 Measures of treatment engagement: DVD arm

Measure	DVD arm (*N* = 244)
Treatment experience score[a]	
n	160
Stomach breathing, median (IQR); minimum, maximum	6 (5–8); 1, 10
Nose breathing, median (IQR); minimum, maximum	6 (5–8); 1, 10
Slow breathing, median (IQR); minimum, maximum	6 (5–8); 1, 10
Controlled breath holding, median (IQR); minimum, maximum	5 (4–7); 1, 10
Relaxation training, median (IQR); minimum, maximum	7 (6–8); 1, 10
Total time spent on each breathing technique,[b] *n* (%)[c]	
Stomach breathing	
Weeks – did not use	10 (4.1)
1–5 weeks	59 (24.2)
≥ 6 weeks	90 (36.9)
Hours – did not use	12 (4.9)
Up to 1 hour	104 (42.6)
Up to half a day or more	41 (16.8)
Nose breathing	
Weeks – did not use	12 (4.9)
1–5 weeks	53 (21.7)
≥ 6 weeks	94 (38.5)
Hours – did not use	13 (5.3)
Up to 1 hour	75 (30.7)
Up to half a day or more	69 (28.3)
Slow breathing	
Weeks – did not use	11 (4.5)
1–5 weeks	64 (26.2)
≥ 6 weeks	85 (34.8)
Minutes – did not use	11 (4.5)
Up to 10 minutes	100 (41.0)
> 10 minutes	48 (19.7)
Controlled breath holding	
Weeks – did not use	19 (7.8)
1–5 weeks	74 (30.3)
≥ 6 weeks	67 (27.5)
Minutes – did not use	20 (8.2)
Up to 5 minutes	103 (42.2)
> 5 minutes	36 (14.8)

TABLE 39 Measures of treatment engagement: DVD arm (*continued*)

Measure	DVD arm ($N = 244$)
Relaxation training	
Weeks – did not use	25 (10.2)
1–5 weeks	59 (24.2)
≥ 6 weeks	76 (31.1)
Minutes – did not use	24 (9.8)
Up to 10 minutes	91 (37.3)
> 10 minutes	45 (18.4)
Treatment engagement score	
n	158
Problems due to symptoms	0 (0–2); 0, 12
Problems due to uncertainty about the therapy	0.5 (0–3); 0, 12
Problems due to doubts about the therapy	1.0 (0–4); 0, 10
Practical problems	6.5 (3–11); 0, 20
Problems due to lack of support	0 (0–3); 0, 12

a Based on different types of breathing retraining.
b Weeks, hours and minutes per day.
c Denominator is those with treatment adherence questionnaire available at 3 months ($n = 244$).

TABLE 40 Summary of serious adverse events/reactions

Event	Treatment arm, *n* (%)			Total ($N = 655$), *n* (%)
	DVD ($N = 261$)	Physiotherapy ($N = 132$)	Usual care ($N = 262$)	
SUSARs	None			
Expected serious adverse reactions	None			
Other serious adverse events	11 (4.2)	4 (3.0)	20 (7.6)	35 (5.3)

SUSAR, suspected unexpected serious adverse reaction.

A summary of the adverse events reported is provided in *Table 42*. A full list of each event reported as well as severity gradings is provided in *Appendix 11*.

Overall, the adverse event profile was as expected in the recruited population, with fewer adverse events in the active arms than in the control arm. There was no indication that any of the adverse events were related to either the DVD programme or the physiotherapy programme, which appeared to be well tolerated.

TABLE 41 Summary of the categories of main symptom(s) reported on the adverse event forms (as categorised by PIs)

Category[a]	Treatment arm, *n* (%)			Total (*N* = 655), *n* (%)
	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	
Abdominal/GIT	19 (35.2)	5 (9.3)	30 (55.6)	54 (100.0)
Acute exacerbation of asthma	32 (45.1)	13 (18.3)	26 (36.6)	71 (100.0)
Chest pain	24 (41.4)	7 (12.1)	27 (46.6)	58 (100.0)
Increased asthma symptoms	29 (29.9)	28 (28.9)	40 (41.2)	97 (100.0)
Malignancy	3 (75.0)	1 (25.0)	0 (0.0)	4 (100.0)
Musculoskeletal	22 (35.5)	15 (24.2)	25 (40.3)	62 (100.0)
Neurological	8 (33.3)	3 (12.5)	13 (54.2)	24 (100.0)
Psychological/psychiatric	12 (28.6)	2 (4.8)	28 (66.7)	42 (100.0)
Respiratory tract infection/cough	79 (35.1)	31 (13.8)	115 (51.1)	225 (100.0)
Rhinitis/rhinosinusitis	20 (43.5)	6 (13.0)	20 (43.5)	46 (100.0)
Miscellaneous	23 (37.7)	12 (19.7)	26 (42.6)	61 (100.0)
Total	271 (36.4)	123 (16.5)	350 (47.0)	744 (100.0)

GIT, gastrointestinal.
a See *Appendix 11* for details of each category.

TABLE 42 Summary of the adverse events reported

Characteristic	Treatment arm			Total (*N* = 655)
	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	
Patients experiencing at least one AE,[a] *n* (%)	101 (38.7)	55 (41.7)	132 (50.4)	288 (44.0)
PI assessment				
Number of AEs	271	123	350	744
Number pending	0	0	0	0
Total number	271	123	350	744
Severity of AE, *n* (%)[b]				
1 – mild	129 (47.6)	66 (53.7)	155 (44.3)	350 (47.0)
2 – moderate	112 (41.3)	44 (35.8)	141 (40.3)	297 (39.9)
3 – severe	25 (9.2)	13 (10.6)	50 (14.3)	88 (11.8)
4 – life threatening	4 (1.5)	0 (0.0)	2 (0.6)	6 (0.8)
5 – death related to AE	1 (0.4)	0 (0.0)	2 (0.6)	3 (0.4)
Pending	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	271 (100.0)	123 (100.0)	350 (100.0)	744 (100.0)

AE, adverse event.
a Denominator is the total number of patients in each arm.
b Denominator is the number of AEs.

Chapter 4 Economic evaluation

Introduction

The health economic analysis evaluated the superiority of each intervention compared with usual care and made a non-inferiority comparison between the DVD arm and the face-to face physiotherapy arm. The ITT population was employed, with imputation of missing values. The time frame was that of the trial. Adjustment was made for baseline values and for repeated measurement. The perspective was that of the NHS, but with exploration of non-NHS costs.

Data collected

Resource use data were collected using three forms. The medication review form was used to record data on all asthma-related NHS consultations and prescriptions over the period of the trial, collected from patient records held by each general practice. It was also used to record outpatient visits, accident and emergency (A&E) visits, out-of-hours consultations and hospital admissions related to asthma. A concomitant medications form was used to record data on six conditions that might be linked to differences in outcomes. A third form was used to record data from patients relating to over-the-counter medications, non-NHS consultations and any other privately accessed items related to asthma or its palliation.

The results presented here relate only to the medication review data. The data on concomitant medications proved unusable for several reasons, principally because of lack of detail provided on relevant medications and dates. The data on patient-reported costs also proved of little use as very few items were recorded. This we interpret as indicating that few such costs were incurred; hence, this justified taking a NHS perspective as opposed to a societal perspective.

Intervention costs

Intervention costs (shown in *Appendix 12*) were £83.45 per patient in the face-to-face physiotherapy breathing retraining group and £2.85 in the DVD breathing retraining group. The physiotherapy group cost was based on the duration of the planned three consultations with the practice nurse, adjusted for attendance. The cost of the DVD intervention was that of printing the discs and documentation. The development cost of these materials was treated as a research cost and was not included here.

Resource use and costs

The unit costs for each of the resource groups (GP consultations, outpatient visits, A&E attendances, out-of-hours consultations, inpatient admissions) and sources are shown in *Appendix 12*.

EuroQol-5 Dimensions and Asthma Quality of Life Questionnaire

Asthma Quality of Life Questionnaire data collection was discussed earlier (see *Chapter 3*). EQ-5D data were collected at the initial visit at baseline and at 3 and 6 months (both by post) and 12 months (assessment visit).

Analyses

Cost–utility analyses were based on all patients randomised. Utility scores were derived based on the UK tariff.[34] QALYs were calculated based on the area under the curve approach. The time frame of the analysis was that of the trial (12 months).

Bootstraps based on 1000 samples with replacements were used to estimate the cost per AQLQ score improvement and cost per QALY gained, with CIs presented to illustrate the uncertainty. Scatterplots are presented to illustrate the uncertainty in the cost–utility estimates.

Results

The medical review form was used to extract patient resource use data in the 12 months following randomisation. Three patients died and two patients left their practice. We assumed that no additional costs were incurred for these patients after the date of their last visit.

The mean NHS cost per patient by treatment arm was aggregated from the costs of asthma-related prescriptions, consultations and hospital admissions. The unadjusted mean cost was highest in the usual-care arm (£356; *Table 43*), with a similar cost in the physiotherapy arm (£335) and the lowest cost in the DVD arm (£296). The main cost items for each group were asthma-related medications and GP consultations, with lower costs reflecting low levels of use of other services; although there were few hospital admissions (usual-care arm, $n = 8$; physiotherapy arm, $n = 0$; DVD arm, $n = 4$), they were by far the most costly item. The numbers of patients using each service are also shown in *Table 43*.

The mean costs in each arm changed only slightly when bootstrap methods were used: £377 in the usual-care arm, £333 in the physiotherapy arm and £293 in the DVD arm (*Table 44*). The differences were not statistically significant at the 5% level.

Given that the intervention costs were higher in the physiotherapy arm (£83.5) and the DVD arm (£2.85) than in the usual-care arm, the inclusion of NHS costs offset these higher costs, leading to lower overall mean costs in both intervention arms than in the usual-care arm.

EuroQol-5 Dimensions data were collected at baseline ($n = 653/655$), 3 months ($n = 519/655$), 6 months ($n = 472/655$) and 12 months ($n = 437/655$) (see *Table 45*). For the whole sample, completion fell from an estimated 99% at baseline to 67% at 12 months. Some participants missed some but not all time points, but data for at least two time point were available for 87% of participants. Linear interpolation was used for those with two or three time points, with imputation for those with fewer time points.

The mean EQ-5D QoL scores varied between 0.751 and 0.826, with small differences at baseline and over time.

The mean EQ-5D QoL scores based on complete cases are shown in *Table 46*.

Cost-effectiveness analysis

The primary analysis of AQLQ score differences was based on the population with baseline measurement of AQLQ scores ($n = 244$, 120 and 246 in the DVD, physiotherapy and usual-care arms respectively; see *Chapter 3*). The cost-effectiveness analyses were based on the same population ($n = 610$ in total).

Bootstrapped mean costs per person in this population were £380 (95% CI £310 to £459), £296 (95% CI £228 to £374) and £334 (95% CI £299 to £269) for the DVD, physiotherapy and usual-care arms respectively.

TABLE 43 Mean NHS resource use in each treatment arm (2014/15 prices)

Resource use	Category	Mean (SD) for those using service	Mean (SD) for all
***Usual care* (N = *262*)**			
Costs (£)[a]	Total costs	379 (672) (*n* = 246)	356 (657)
	Medication	183 (217) (*n* = 242)	169 (214)
	GP consultation	100 (84) (*n* = 201)	77 (85)
	Outpatient attendance	347 (321) (*n* = 21)	28 (130)
	Hospital admission	2581 (0) (*n* = 8)	79 (445)
Number of cases	Medication usage	9.71 (10.14) (*n* = 242)	8.97 (10.08)
	GP consultation	2.22 (1.87) (*n* = 201)	1.71 (1.89)
	Outpatient attendance	2.57 (2.38) (*n* = 21)	0.21 (0.96)
	Hospital admission	1 (0) (*n* = 8)	0.03 (0.17)
***Physiotherapy* (N = *132*)**			
Costs (£)[a]	Total costs	335 (254) (*n* = 132)	335 (254)
	Medication	173 (199) (*n* = 120)	157 (196)
	GP consultation	92 (93) (*n* = 99)	69 (90)
	Outpatient attendance	203 (88) (*n* = 14)	21 (68)
	Hospital admission	0 (0) (*n* = 0)	0 (0)
	Intervention	83 (0) (*n* = 132)	83 (0)
Number of cases	Medication usage	9.27 (7.49) (*n* = 120)	8.42 (7.63)
	GP consultation	2.04 (2.07) (*n* = 99)	1.53 (2)
	Outpatient attendance	1.5 (0.65) (*n* = 14)	0.16 (0.51)
	Hospital admission	0 (0) (*n* = 0)	0 (0)
	Intervention	1 (0) (*n* = 132)	1 (0)
***DVD* (N = *261*)**			
Costs (£)[a]	Total costs	296 (715) (*n* = 261)	296 (715)
	Medication	167 (177) (*n* = 222)	142 (174)
	GP consultation	94 (99) (*n* = 186)	67 (94)
	Outpatient attendance	221 (122) (*n* = 25)	21 (75)
	Hospital admission	3872 (2581) (*n* = 4)	59 (551)
	Intervention	3 (0) (*n* = 261)	3 (0)
Number of cases	Medication usage	9.04 (8.03) (*n* = 222)	7.69 (8.08)
	GP consultation	2.08 (2.2) (*n* = 186)	1.48 (2.08)
	Outpatient attendance	1.64 (0.91) (*n* = 25)	0.16 (0.56)
	Hospital admission	1.5 (1) (*n* = 4)	0.02 (0.21)
	Intervention	1 (0) (*n* = 261)	1 (0)

Note

a All costs consist of the total costs incurred. The main components of all costs were the services shown, that is, GP consultations, medications, hospital admissions and the intervention.

TABLE 44 Total costs per person using bootstrap methods

Treatment arm	Cost (£), mean (95% CI)	Incremental cost (£), mean (95% CI)
Usual care	377 (310 to 459)	–
Physiotherapy	333 (299 to 369)	–41 (–134 to 33)
DVD	293 (228 to 374)	–83 (–187 to 12)

TABLE 45 Mean EQ-5D scores over 12 months in each treatment arm based on complete cases

Time	EQ-5D score, mean (SD)	Number completing	% completion
***Usual care* (n = *262*)**			
Baseline	0.805 (0.236)	261	100
3 months	0.773 (0.269)	222	85
6 months	0.751 (0.301)	212	81
12 months	0.797 (0.246)	191	73
***Physiotherapy* (n = *132*)**			
Baseline	0.794 (0.269)	130	98
3 months	0.789 (0.275)	105	80
6 months	0.774 (0.272)	98	74
12 months	0.747 (0.318)	93	70
***DVD* (n = *261*)**			
Baseline	0.82 (0.235)	258	99
3 months	0.775 (0.275)	167	64
6 months	0.794 (0.269)	162	62
12 months	0.826 (0.221)	153	59

TABLE 46 Mean EQ-5D scores based on complete cases

Treatment arm	EQ-5D score, mean (95% CI)	Number of patients with complete data at all points	Percentage used in the calculation
Usual care ($n = 262$)	0.801 (0.765 to 0.836)	154	58.8
Physiotherapy ($n = 132$)	0.764 (0.696 to 0.831)	70	53.0
DVD ($n = 261$)	0.817 (0.776 to 0.858)	113	43.3

This gave a difference in costs of –£83 (95% CI –£187 to £12) for the DVD arm and –£45 (95% CI –£134 to £33) for the physiotherapy arm compared with the usual-care arm (*Table 47*).

The estimated differences in AQLQ scores, based on bootstrap methods with adjustments for prespecified covariates, were similar to those in the primary analyses, with differences of 0.23 (95% CI 0.06 to 0.40) for the physiotherapy arm compared with the usual-care arm and 0.26 (95% CI 0.11 to 0.41) for the DVD arm compared with the usual-care arm (see *Table 47*).

TABLE 47 Incremental cost per AQLQ score improvement (ICER) based on imputed data

Treatment arm	Cost (£), mean (95% CI)	Difference in costs (£), mean (95% CI)	Difference in AQLQ score, mean (95% CI)	Incremental cost (£) per AQLQ score improvement (95% CI)
Usual care ($n = 246$)	380 (310 to 459)			
DVD ($n = 244$)	296 (228 to 374)			
Physiotherapy ($n = 120$)	334 (299 to 269)			
Physiotherapy vs. usual care		–45 (–134 to 33)	0.23 (0.06 to 0.40)	–400 (–1545 to 106)
DVD vs. usual care		–83 (–187 to 12)	0.26 (0.11 to 0.41)	–340 (–986 to 52)

The incremental cost per AQLQ score improvement was –£400 (95% CI –£1545 to £106) for the physiotherapy arm compared with the usual-care arm and –£340 (95% CI –£986 to £52) for the DVD arm compared with the usual-care arm (see *Table 47*). Both interventions dominated usual care. Given the non-inferiority of the DVD intervention compared with the physiotherapy intervention, cost-minimisation analysis favoured the DVD intervention over the physiotherapy intervention. This was the base case for the cost-effectiveness analysis.

Cost–utility analysis

Incremental differences between the arms in terms of costs and QALYs and the incremental cost-effectiveness ratios (ICERs) are shown in *Table 48*. There were small baseline adjusted QALY differences between the arms, with the face-to-face physiotherapy arm having 0.007 more QALYs than the usual-care arm and the DVD arm having 0.02 more QALYs than the usual-care arm. The DVD arm showed a gain of 0.014 QALYs compared with the face-to-face physiotherapy arm. The gains were not statistically significant.

In the adjusted analysis (bottom part of *Table 48*), the ICERs had negative values for both the physiotherapy arm and the DVD arm compared with the usual-care arm. The physiotherapy arm cost £877 less per QALY than the usual-care arm and the DVD arm cost £3057 less per QALY than the usual-care arm. Both interventions dominated usual care. The CIs for these ICERs were wide and not statistically significant. Similar results were found in the unadjusted analysis.

The probability of dominance was investigated for each of the comparisons. This can be interpreted as the proportion of the simulated results (points on a scatterplot) that fall into the lower right-hand (south-east) quadrant. Scatterplots are shown of the joint distribution of the incremental mean cost and mean QALYs for the DVD arm compared with the usual-care arm (*Figure 6*) and for the physiotherapy arm compared with the usual-care arm (*Figure 7*).

The probability of usual care being dominated by the DVD intervention (lower costs and higher QALYs) was 82%. The probability of usual care being dominated compared with the face-to-face physiotherapy intervention (lower costs and higher QALYs) was 51%.

Discussion and conclusions

This well-conducted randomised trial provides evidence of the likely cost-effectiveness of both face-to-face physiotherapy and breathing retraining delivered using a DVD and booklet. Limitations include the time frame used, the reliance of the cost-effectiveness estimates on a single trial and the restriction of the

TABLE 48 Costs, QALYs and incremental cost per QALY (ICERs) using bootstrap methods based on imputed data

Treatment arm	Cost (£), mean (95% CI)	Incremental cost (£), mean (95% CI)	QALYs, mean (95% CI)	Incremental QALYs, mean (95% CI)	ICER (£/QALY) (95% CI)
Usual care	377 (310 to 459)		0.767 (0.738 to 0.79)		
Physiotherapy	333 (299 to 369)	–41 (–134 to 33)	0.771 (0.735 to 0.807)	0.005 (–0.039 to 0.05)	–671 (–14,269 to 13,814)
DVD	293 (228 to 374)	–83 (–187 to 12)	0.788 (0.764 to 0.811)	0.022 (–0.013 to 0.058)	–2754 (–17,739 to 12,017)
DVD vs. physiotherapy		40 (–43 to 116)		0.017 (–0.025 to 0.06)	–941 (–12,260 to 11,620)
Treatment arm	**Cost (£), mean (95% CI)**	**Incremental cost (£) (95% CI)**	**QALYs adjusted for baseline QoL, mean (95% CI)**	**Incremental adjusted QALYs (95% CI)**	**ICER (£/adjusted QALY) (95% CI)**
Usual care	377 (310 to 459)		0.767 (0.741 to 0.788)		
Physiotherapy	333 (299 to 369)	–41 (–134 to 33)	0.773 (0.74 to 0.805)	0.007 (–0.033 to 0.047)	–877 (–15,555 to 18,573)
DVD	293 (228 to 374)	–83 (–187 to 12)	0.787 (0.765 to 0.807)	0.02 (–0.011 to 0.053)	–3057 (–18,877 to 10,864)
DVD vs. physiotherapy		40 (–43 to 116)		0.014 (–0.023 to 0.052)	–1145 (–14,982 to 9843)

Note
The mean incremental costs and QALYs and ICERs between two treatment arms are not directly derived from the mean cost and mean QALYs in each group because of the bootstrap methods used.

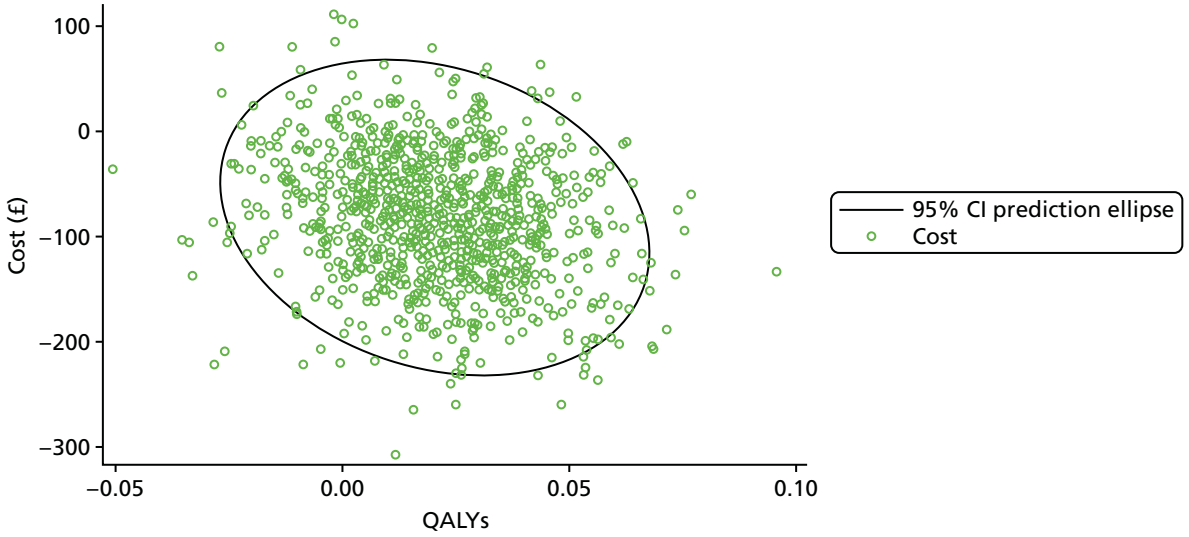

FIGURE 6 Scatterplot of the joint distribution of the incremental mean cost from a NHS perspective and mean QALYs adjusted for baseline QoL over 12 months based on the imputed data: 95% CI ellipse DVD arm compared with the usual-care arm.

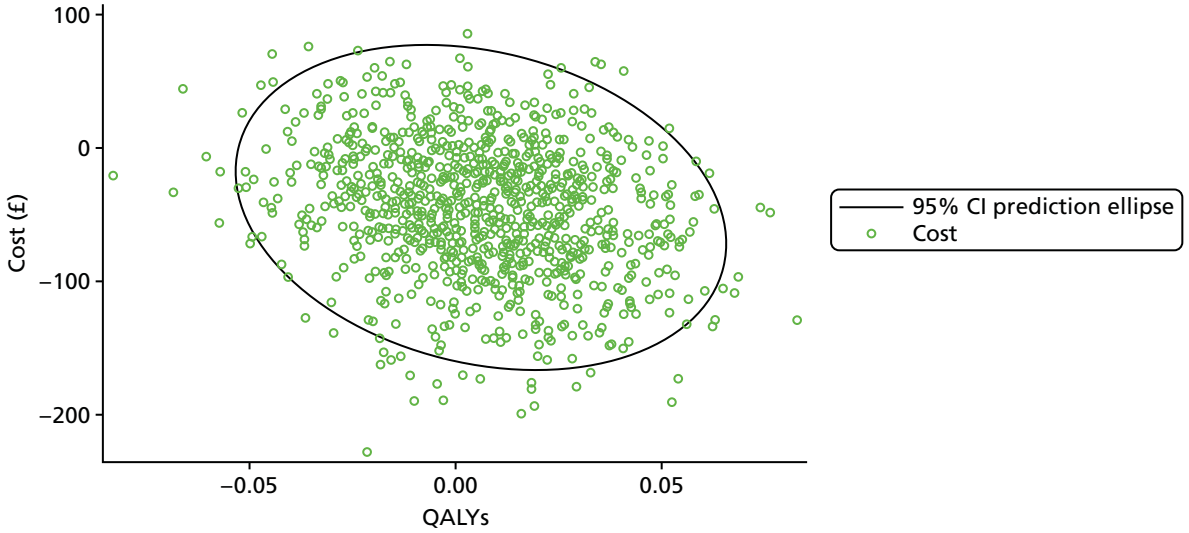

FIGURE 7 Scatterplot of the joint distribution of incremental mean cost from NHS perspective and mean QALYs adjusted baseline QoL over 12 months based on the imputed data: 95% CI ellipse physiotherapy arm compared with the usual-care arm.

costing perspective to the NHS. Although longer-term follow-up would be desirable, it seems likely that patients who have been able to improve their QoL using breathing retraining would continue to apply the techniques that they have learned. If so, the benefits recorded here may have been understated. Although cost-effectiveness should ideally be based on the totality of evidence, such as a meta-analytical estimate of effect size, we note similar results for the one similar trial of breathing exercises in asthma.[17] Our adoption of a NHS, as opposed to a societal, perspective was based on the returns from a questionnaire, which indicated that few costs fell outside the NHS.

The cost/AQLQ analysis favoured both the DVD intervention and the face-to-face physiotherapy intervention compared with usual care, with the DVD intervention achieving equivalent outcomes to the face-to-face physiotherapy intervention at a lower cost. The cost/QALY analysis showed similar results for the DVD and face-to-face physiotherapy comparisons with usual care, albeit based on small non-significant differences in outcomes. Both interventions dominated usual care. The DVD intervention had similar outcomes to the

face-to-face physiotherapy intervention but at lower costs. The probabilities of the interventions being dominant were 85% for the DVD intervention compared with usual care and 51% for the face-to-face physiotherapy intervention compared with usual care. Thus, both the cost-effectiveness analysis and the cost–utility analysis provided congruent results. Both interventions achieved outcome gains at lower total costs than usual care. The lower cost in the DVD group meant that the DVD intervention was preferable to face-to-face physiotherapy. The low cost of the DVD (£2.85) meant that, if effective, it was highly likely to be cost-effective. Further, if made available on the internet, its cost would fall to close to zero.

In conclusion:

- the QALY differences between the treatment arms were in the same direction as the differences in the primary outcome, but were smaller
- the increased cost of each intervention was offset by reductions in total costs so that both interventions dominated usual care
- the DVD/booklet training was preferable to face-to-face physiotherapy, as the outcomes were within the equivalence margin and the DVD intervention had a lower cost.

Chapter 5 Intervention development

The BREATHE trial was a three-armed trial, with two active arms and one control arm. The active arms consisted of physiotherapy breathing retraining delivered face-to-face and physiotherapy breathing retraining delivered using a DVD, with an accompanying booklet (*Breathe Freely*) provided to both active arms. This chapter describes the process of developing these three intervention components prior to carrying out the pilot RCT.

Face-to-face physiotherapy

Although breathing retraining for asthma is provided by some physiotherapists within the NHS and privately, in clinical practice there may be considerable variation in the content and frequency of face-to-face sessions. For this research we needed to standardise the intervention as much as possible to ensure that each participant received similar treatment and potentially to allow for comparability across different therapists. Our initial plan was to recruit two to three part-time physiotherapists to provide the face-to-face intervention during the life of the BREATHE trial.

The first step was to decide on the frequency of sessions. In clinical practice, physiotherapists have the option to tailor their treatments to the needs of individual patients, which results in large variations in treatment session numbers from patient to patient. However, previous related research trials by the chief investigator[17,19] had demonstrated that three face-to-face sessions were sufficient to have a positive effect on the primary outcome, and discussions with local physiotherapists also suggested that three was the average number of sessions provided within the NHS. It was therefore decided that all participants should be offered three sessions with the physiotherapist, with intervention adherence being predefined as attending any two out of these three sessions.

The content for each session was derived from discussions with physiotherapists, from AB's own experience and from discussion with other members of the research team. From these discussions, AB produced two documents: a complete description of the protocol for face-to-face physiotherapy [*Face-To-Face Physiotherapy Protocol* (Anne Burton, University of Southampton, 2012)] and a reduced version of the protocol to be given to intervention physiotherapists during training workshops [*Training Manual for Physiotherapists* (Anne Burton, University of Southampton, 2012)].

Training workshops were held by AB at various locations, at which the physiotherapists received information about the trial and the training manual. Details of the training provided at these workshops can be found in the manual. Although five physiotherapists attended these workshops, ultimately, only one physiotherapist (Ruth DeVos) provided all of the intervention sessions throughout the life of the trial. Fidelity of intervention delivery was determined in two ways: first, by the physiotherapist completing specifically designed checklists (see the *Face-To-Face Physiotherapy Protocol* for details) and, second, through the use of direct observation, whereby AB went out to the general practices during both the pilot trial and the main trial to observe the physiotherapist delivering a session of the intervention for approximately 5% of the participants (6 out of the 132 recruited to this arm). There was 100% adherence to the intervention protocol by the physiotherapist (physiotherapist adherence to the protocol had been predefined as conforming to 90% of the checklist).

Booklet development (*Breathing Freely*)

Previous experience from within the research team had indicated that accompanying materials (such as a written booklet) containing behavioural content to motivate and reassure patients were very useful to support user self-management.[35] Our booklet, *Breathing Freely: Your Guide to Breathing Retraining for Asthma*, was developed by a team of health psychologists, physiotherapists, physicians and patient representatives

(Emily Arden-Close, Sarah Kirby, Emma Teasdale, Anne Bruton, Mike Thomas, Mark Stafford-Watson, Denise Gibson, Lucy Yardley, University of Southampton, 2013).

A draft booklet was first created by three of the authors (EAC, LY), based on advice from physiotherapists (AB, DG) and a GP with expertise in asthma (MT) and a similar booklet that LY had created that had successfully supported the exercise-based self-management of symptoms in patients with dizziness.[35] The first part of the booklet (pages 1–8) was designed to build motivation (in terms of social cognitive theory and positive outcome expectancies) and confidence (self-efficacy) to undertake breathing retraining. To convince users that breathing retraining would be effective, the cognitive–behavioural rationale for breathing retraining was first explained in terms of the vicious cycle of breathing problems, anxiety and hyperventilation and how this could be reversed by breathing retraining. Positive expectancies for treatment benefit were promoted by explaining how breathing retraining can improve not only breathing but also psychological well-being, and can allow users to do more without becoming breathless. The second part of the booklet (pages 10–15) contained detailed instructions (with illustrations) on how to progressively master breathing retraining, with reassurance and advice addressing common difficulties and barriers. The final part of the booklet (pages 16–21) encouraged users to use their new breathing skills to engage in more daily activities that they might have previously found difficult because of asthma (e.g. exercise, stressful situations). Implementation of breathing retraining was encouraged by providing success stories from other patients and charts to plan when to carry out the breathing exercises and physical activity and log progress.

Using our 'person-based approach' to developing accessible, persuasive and helpful intervention materials,[36] feedback on the draft version was sought through the use of semistructured think-aloud interviews lasting approximately 1 hour with 29 people with asthma. The interviews included two components: open-ended questions exploring attitudes to breathing retraining exercises in the context of health beliefs and lifestyle and think-aloud methods to elicit spontaneous reactions to the booklet. Interview questions covered participants' experiences of managing their asthma. This included questions about breathing difficulties, previous experience of breathing techniques for asthma management and the perceived relevance of breathing training exercises to asthma control. Participants then read the draft booklet and provided feedback about each page. Further open-ended questions explored impressions of the booklet, attitudes to breathing exercises, perceived attitudes of relevant others (family, health-care professionals), barriers to carrying out breathing exercises at home and possible ways of overcoming these barriers.

After each interview the feedback on each page was tabulated into recommended changes and positive aspects of the booklet. After the first few interviews had been conducted, the recommended changes were collated and a MoSCoW (must, should, could, would) analysis was conducted (breaking changes down into things we must, could, should and were not going to do), based on the nature of the comments and how many people mentioned each comment. The booklet was then revised before further interviews were conducted. This cycle continued until no further major changes were suggested. Further details of this process and the changes made in response to feedback can be found in two publications.[36,37]

DVD development

Our aim was to produce an intervention that replicated the experience of face-to-face physiotherapy breathing retraining in an accessible self-guided format. We acquired the media in a high-quality video file format to 'future-proof' our content as much as possible and facilitate distribution using different technologies. The available technologies for distribution at the time of the original funding application were videotape, DVD and the internet. Although we knew that distributing video via the internet was possible, we chose the DVD as the distribution format for this project because, at the time, DVD players were becoming more popular and fewer people in the UK had access to the internet. In 2009 (when the funding application was written) the broadband network and hardware required to view internet-distributed video was not established or as widespread as it is now. Since then, distributing video via the internet has become ubiquitous. Reformatting our original video files for distribution via the internet will be relatively straightforward.

To enable people to identify with the patients seen on screen on the DVD, it was decided to involve genuine individuals with asthma (rather than actors) to take on the roles of patients. A local specialist respiratory physiotherapist (Denise Gibson) was asked to play the role of the breathing retraining physiotherapist. Dr Mark Porter (who has considerable experience of fronting medical programmes on both radio and television) kindly agreed to be the 'presenter' for the DVD.

The DVD production team consisted of AB, MT and DG, the psychology team developing the booklet, patient representatives, a commercial company (Zemedia) and staff at Solent University Studios, Southampton. AB produced a draft script for the DVD, based on a combination of the written Face-To-Face Protocol, the developing *Breathing Freely* booklet and discussions with physiotherapists. This was then shared with our psychology team members, patient representatives and others in the research team. Input from TMG patient representatives was of great importance in these revisions, and these representatives were involved in and commented on all revision steps, providing verbal and written comment on patient perspectives of the intervention. In addition, the iterative person-based think-aloud process for the development of digital behavioural interventions that was used in the development process for this intervention (described in detail in *Chapter 6*) used a representative sample of 29 adults with asthma purposively sampled for diversity of age, sex, education and symptom profile. These patients looked at draft versions of the intervention and provided feedback and comment using a formal qualitative methodology, and this was used to modify the intervention based on their reactions and comments. Several revisions to the script were subsequently made in response to comments and feedback from within the team. A professional media production team (Zemedia) had been identified by AB in 2009 during the initial funding application process and its main representative (Tim O'Riordan) had been regularly attending project meetings from 2011. Zemedia were employed to translate our script into a filmable story, to film the scenes and to create and produce the final DVD. Script refinement and preparation for filming continued over the first year of the research programme, during which period there were several team meetings to agree on patient roles and locations and to design 'story boards' for individual scenes. Filming took place over 3 days in May and June 2012, in Solent University Studios and on location in patients' homes, with Steve Bowles of Zemedia and AB directing. Clips from the filming were shared within the research team for comment in terms of what to include/exclude, what voiceovers were appropriate and general formatting of the DVD. It was not felt appropriate to seek patient feedback on the developing DVD itself at that stage as it would not have been possible to refilm scenes because of time and financial constraints. Tim O'Riordan was responsible for the editing and post-production work that resulted in the final version of the DVD used in the trial. Feedback on the DVD as used by participants was sought as part of the research trial and is described elsewhere in this report.

Patient and public involvement (PPI) was central to this project, with two PPI representatives on the TMG attending TMG meetings and commenting on all stages of the process, and with the patient charity Asthma UK being a partner in the process. With the partnership of the charity and the active involvement of patients in all stages of the trial, in particular in the development and optimisation of the DVD intervention and booklet, we feel that there was complete PPI involvement overall. We did not experience any difficulty in obtaining PPI or in acting on it and would recommend that further trials in this clinical area integrate PPI into their processes as much as possible and involve patient charities if possible.

Chapter 6 Process evaluation

In line with Medical Research Council (MRC) guidance for developing and evaluating complex interventions[38] and the MRC process evaluation framework,[39] qualitative and quantitative process evaluations were nested within the trial to allow for a more detailed exploration of aspects that may be relevant to trial outcomes that might inform policy and practice. The qualitative process evaluation was conducted after the BREATHE trial 3-month follow-up with a sample of participants who had taken part in the intervention arms of the trial, to capture their perspectives on the interventions and understand what aspects were perceived as strengths and weaknesses.

The aim of the quantitative process evaluation was to explore participants' reported expectations of the interventions, their experiences and their level of engagement with the interventions. Measures for the quantitative process evaluation were taken immediately after randomisation and at each of the 3-month, 6-month and 12-month follow-up time points. Like the qualitative process evaluation, only those who had taken part in the intervention arms of the trial were included.

The methodology and findings of the qualitative and quantitative process evaluations are each reported in more detail in the following sections.

Qualitative process evaluation

The qualitative process evaluation aimed to explore the experiences of participants in the intervention arms (DVD and face-to-face physiotherapy) of the BREATHE trial, to understand what patients perceive as the strengths and weaknesses of the different modes of delivery of breathing retraining.

Methodology

Semistructured telephone interviews were used to explore participants' experiences of breathing retraining for asthma delivered by DVD or face-to-face physiotherapy. Participants were eligible for inclusion if they had taken part in one of the two intervention arms of the trial. Initially, consecutive sampling of participants in the pilot for the main trial was used. Purposive sampling was used towards the end to ensure adequate representation of male participants. Recruitment continued until the data reached saturation (i.e. no new themes were being raised). The final sample consisted of 11 women and five men between the ages of 23 and 70 years [mean (SD) age 55.2 (12.9) years]. There were eight participants (two men) in the DVD group and eight participants (three men) in the face-to-face physiotherapy group.

The transcripts were analysed by EAC using inductive thematic analysis. Transcripts were read carefully several times to ensure familiarity with the data. A coding manual was developed on the first few transcripts to ensure transparent and systematic coding of data and this was frequently revised. Themes were continually compared with newly coded transcripts to ensure that they applied to the data. The coding manual was then checked with LY and a sample of texts second coded, to ensure good inter-rater reliability. Themes were checked for differences as a function of group (intervention arm).

Results

Five main themes emerged: reasons for taking part, experience of breathing retraining, impact of breathing retraining, benefits of breathing retraining and problems with breathing retraining. These are discussed in the following sections.

Reasons for taking part

Reasons for taking part included being asked to, to enhance progress in research, to feel better/reduce symptoms and to reduce the use of medication. Some participants took part because a health-care professional asked them to:

> *I had my um annual asthma check-up and they just asked me if I would do it kind of there and then so I just said that I would.*
>
> *P9, female, DVD*

Some participants had always supported research and felt that it was their duty to give something back to help enhance progress with regard to research and knowledge:

> *because I would support research that is going to improve things for human beings.*
>
> *P16, male, face-to-face physiotherapy*

Many participants felt that it would help improve their health and symptoms:

> *I was just hoping it would . . . help my breathing when I went up hills . . . because that's what I was particularly concerned with.*
>
> *P2, female, DVD*

Related to this, many participants wanted to reduce their use of medication. Although they took it as required, they wanted to be less dependent on it:

> *I liked the idea of a natural solution to the asthma rather than having to take medication.*
>
> *P4, female, face-to-face physiotherapy*

Experience of breathing retraining

The participants in the face-to-face group had a positive impression of the physiotherapist, who tailored the treatment to their needs, and found the sessions motivational.

All of the participants in the face-to-face group had a positive impression of the physiotherapist as friendly, very helpful, supportive and patient:

> *the lady that did them was really, really nice. She wasn't condescending in any way, she was really patient, she was very quick to praise when you did it right.*
>
> *P14, female, face-to-face physiotherapy*

Participants mentioned that the physiotherapist tailored the treatment to their needs, rather than offering a 'one size fits all' approach. When they were experiencing difficulties, she reviewed the techniques and helped to break down goals into more manageable ones. For example, one participant described this experience of improving nose breathing:

> *When I spoke to [the physiotherapist] about it um, originally because I was having problems with it, she said just try and set myself little goals. So what I sort of do is when sort of leave the house I sort of set myself a goal to breathe through my nose to a certain point and then I will do it again, you know, I will get to this point and then I will try and breathe through my nose again.*
>
> *P5, female, face-to-face physiotherapy*

The physiotherapist also tailored support as participants needed, which facilitated mastery of the techniques:

> *. . . when she said, 'Now, I need you to do these exercises at home', she saw the look on my face and she said, 'Would you like me to write the instructions down?' And I said, 'Yes, please'. And so that,*

> *because I'd already done the actual training bit in my session the instructions put it back into my mind what I had to do and I found it really, really informative.*
>
> *P14, female, face-to-face physiotherapy*

The face-to-face physiotherapy group also found seeing the physiotherapist motivational. Knowing that they would attend appointments prompted them to prioritise practising breathing techniques:

> *I liked having the person there. It is not so much that she told me off when I hadn't done the exercises but it is like an extra conscience.*
>
> *P5, female, face-to-face physiotherapy*

The materials used by participants in the DVD group (booklet and DVD) were also considered useful. Participants liked the booklet as it reminded them to carry out their exercises, was helpful to refer to when practising and enabled them to log results. Participants also found that the DVD helped when practising the exercises. However, although some preferred the DVD because it showed them how to perform the exercises, some preferred the booklet because it could be carried anywhere:

> *. . . with the DVD it was actually showing you.*
>
> *P11, male, DVD*

> *I liked the booklet better . . . because I could just pick it up and, you know, look at it and um do some of the exercises when I wanted to.*
>
> *P2, female, DVD*

Generally, participants felt that the booklet and the DVD complemented each other:

> *I found by reading the booklet and then watching the DVD the two matched and I could see what was meant.*
>
> *P13, female, DVD*

Impact of breathing retraining

The three main ways that participants felt that their lives were impacted by breathing retraining were in undergoing regular practice, having an increased awareness of breathing and developing new habits. Many participants reported initially practising breathing techniques regularly (more than three times a day), in line with recommendations, and felt that this had facilitated development of new habits. Also, many mentioned increased awareness of their breathing. Talking to the physiotherapist or watching the DVD and practising the exercises made them aware that they had been breathing incorrectly:

> *I'm a habitual mouth breather and to realise that I'd been breathing wrong all my life was a bit of an eye opener.*
>
> *P10, female, face-to-face physiotherapy*

> *I do try to make myself aware of breathing through my nose all the time.*
>
> *P11, male, DVD*

Many participants mentioned being able to perform stomach breathing and nose breathing automatically. They had internalised this new way of breathing so it became a habit:

> *I can at rest actually do the stomach breathing pretty much naturally now.*
>
> *P3, female, DVD*

> *I still try and do it [nose breathing].*
>
> *P12, male, face-to-face physiotherapy*

Benefits of breathing retraining

Participants also mentioned many health benefits that they associated with breathing retraining, including increased control over breathing, reduced need for medication, feeling more relaxed and improved health and QoL. Almost all participants mentioned increased control over breathing. They reported being able to use the techniques to breathe through asthma attacks:

> *I had two asthma attacks last year . . . and um actually being able to do this breathing helped a lot and I didn't have to go to hospital.*
>
> *P14, female, face-to-face physiotherapy*

Related to this, breathing retraining was often associated with a reduced need for medication. Many participants were able to use breathing techniques rather than reaching for a reliever inhaler when they felt symptoms coming on:

> *I don't have to keep getting my inhaler and taking my inhaler um, I can literally just um do some of these breathing and I feel much better.*
>
> *P5, female, face-to-face physiotherapy*

Participants also mentioned that the breathing techniques helped them to relax:

> *. . . when things have got a bit busy I have sort of been very conscious to do it and I've found it very helpful and very calming.*
>
> *P15, male, face-to-face physiotherapy*

Other benefits attributed to breathing retraining under the umbrella of improved health and QoL included being less wheezy, sleeping better and having more energy:

> *I sleep so much better.*
>
> *P14, female, face-to-face physiotherapy*

> *I also used to get very wheezy first thing in the morning and that doesn't seem to be happening now.*
>
> *P3, female, DVD*

Problems with breathing retraining

Participants also mentioned problems with breathing retraining. These included difficulties finding time to practise and difficulties mastering techniques. Many participants said that it was difficult to find time to practise the breathing techniques before they were able to fit them fitted into their daily routine:

> *Initially quite hard to get started. It was finding the time I think um and putting aside a regular time so that I didn't skip things.*
>
> *P13, female, DVD*

Barriers included busy schedules and difficulties trying to fit the exercises in during the daytime while at work, meaning that high levels of motivation were required to carry them out:

> *I could do as many BREATHE's in the evening when I'm sat at home . . . but finding the time throughout the day when I'm at work, that was a bit more challenging.*
>
> *P5, female, face-to-face physiotherapy*

Many participants also mentioned difficulties with mastering the techniques. Many participants found breath holding most difficult:

> *. . . the most difficult I found holding my breath.*
>
> *P4, female, face-to-face physiotherapy*

Ease of mastering the techniques varied. Participants usually found it easier to carry out the techniques if they had previous experience of them. Apart from one participant in the face-to-face group who experienced severe problems with breath holding, an inability to carry out the techniques appeared more common in the DVD group:

> *I have to say um, no matter how I tried, and on the DVD it said it would come eventually, I cannot breathe through my diaphragm.*
>
> *P7, female, DVD*

Some participants found it difficult to apply the techniques in particular situations:

> *I can't quite master the stomach breathing when I am moving around, but no doubt that will come.*
>
> *P3, female, DVD*

Discussion

Reasons for taking part in the BREATHE trial included being asked to, to enhance progress in research, to feel better/reduce symptoms and to reduce medication use. Participants in the face-to-face group had a positive impression of the physiotherapist, liked receiving treatment tailored to their needs and found meetings motivational. All participants liked the materials. The impact of breathing retraining included regular practice of the exercises leading to increased awareness of breathing and the development of new habits. The perceived benefits of breathing retraining included increased control over breathing, a reduced need for medication, feeling more relaxed and improved health and QoL. However, problems included difficulties in finding time to practise and with mastering techniques.

Strengths and limitations of the study

This is the first full analysis of patients' experiences of breathing retraining for asthma self-management. However, it has several limitations. Although participants were randomised to their treatment arm of the trial, they self-selected into this nested qualitative process evaluation. Despite attempts to reduce socially desirable responding, participants may have felt pressure to report positive outcomes. In addition, the interviewer may have brought bias from being involved in creating the intervention, although participants were unaware of this.

Interpretation of the findings in relation to previously published work

There was very little intentional non-engagement in breathing retraining. Participants wanted to improve their asthma control and reduce their reliance on medication. Previous research has also shown that people with asthma adopt non-pharmacological methods of management to reduce reliance on medication.[37,40] Most participants reported practising intensively (more than three times a day) for the initial 3–4 weeks, as recommended by the physiotherapist and in the booklet. Following this, participants reported increased awareness of their breathing and that breathing techniques had become habitual, in line with research showing that habit formation is an effective health behaviour change strategy.[41]

Participants in the face-to-face group were very positive about the physiotherapist. Many said that the meetings motivated them to carry on with their exercises, with participants in the DVD group stating that they would have preferred to see the physiotherapist. Similarly, in a trial of vestibular rehabilitation for dizziness delivered with or without telephone support, all participants reported preferring telephone support.[42] A reported inability to master certain techniques appeared to be more common in the DVD group. Although many face-to-face physiotherapy participants mentioned finding diaphragm breathing, breath holding and slow breathing difficult initially, several in the DVD group reported being unable to master diaphragm breathing. Those who saw the physiotherapist said that she had tailored the treatment to their needs and they felt able to improve with this support and encouragement. However, the BREATHE trial showed that face-to-face physiotherapy was only marginally more effective than the DVD. Similarly, in a trial of vestibular rehabilitation, telephone support did not lead to greater improvements than a booklet.[35] Although personal contact may enhance confidence in carrying out techniques, this does not necessarily

lead to greater benefits. However, a minority of individuals may need face-to-face instruction to master novel techniques. The perceived benefits of breathing retraining included better asthma control, meaning that participants were able to breathe their way through asthma attacks and, in some cases, possibly even avoid hospital admissions; reduced use of reliever medication, meaning that participants felt more in control of their asthma and less worried if an inhaler was not available; feeling more relaxed; and sleeping better. Participants also reported having more energy and feeling better. These benefits are similar to those found in previous breathing retraining trials.[3,17] Many participants reported difficulties with finding time to perform the breathing exercises until they were able to make them part of their routine. One participant reported dropping out of the trial because of difficulty finding time to practise. People who saw the booklet during the development phase predicted that it would be difficult for those working full-time and/or with young children to find time to practise the exercises.[37] However, in contrast to previous findings,[37] all participants saw the relevance of breathing retraining, possibly because the trial was open only to those whose QoL was affected by asthma.

Implications for health care and recommendations for research

Breathing retraining was well received by participants in both groups, with many reporting improved well-being, and is likely to be acceptable and valued as an adjuvant treatment in general practice, whether delivered face-to-face or by DVD. Given the greatly increased availability of DVD delivery, plus the limited increased benefit provided by face-to-face physiotherapy, making the breathing training DVD (and booklet) widely available may lead to improved asthma control in the general population. This could be tested in a large-scale RCT. To increase the confidence of individuals carrying out breathing retraining delivered by DVD, it might be helpful to inform them that research has demonstrated equivalent benefit of the DVD delivery method to face-to-face physiotherapy. Also, individuals offered breathing retraining delivered by DVD could be provided with a telephone number to contact in case they experienced difficulties in mastering the techniques, to enhance the benefits of breathing retraining. Overall, though, breathing training is likely to be well received as a method of asthma management.

Quantitative process evaluation

The objective of the quantitative process evaluation was to quantify patient-reported expectations of treatment, experiences of treatment and engagement. This process evaluation included five main sets of analyses:

1. Sensitivity analyses – of engagement with and amount of practice of the BREATHE exercises reported at 3 months' follow-up. The rationale for these analyses was to assess treatment efficacy in participants who met 'threshold engagement' levels; that is, efficacy is expected to be greater in those who have looked at the DVD/booklet and carried out breathing retraining at least once, and to investigate whether participants who practised the exercises more regularly derived more benefit.
2. Between-group differences – to explore whether there was a difference between the two intervention groups on measures of expectancy, experience, treatment engagement and practical barriers.
3. Predictors of the amount of practice and continuous engagement – to assess whether expectancy, experience and practical barriers are associated with the amount of practice (at 3 months) and continuous engagement (at 6 and 12 months).
4. Analyses were carried out to model the theory of planned behaviour and explore whether intentions, the amount of practice, engagement and continued engagement can be predicted by the model.
5. The factor structure of the Problematic Experiences of Therapy Scale (PETS)[43] was checked using exploratory factor analysis as it has not previously been used in an asthma population.

Methodology

Immediately after randomisation, participants in the two intervention groups (DVD or face-to-face physiotherapy) were shown the booklet and asked to complete a questionnaire assessing expectancy (their beliefs about asthma and their first impressions of the intervention to which they had been

allocated). At the 3-month follow-up, participants in the two intervention groups were asked to complete brief questionnaires relating to their experiences of treatment, engagement with treatment and perceived barriers to carrying out the treatment. Questions to assess whether or not participants continued using the two treatments were included at the 6- and 12-month follow-ups.

Measures

Expectancy (baseline)

Beliefs about asthma

- *Perceived causes*. A single item from the Brief Illness Perceptions Questionnaire (IPQ) was used.[44] People with asthma commonly attribute the cause of their asthma to external factors such as being hereditary or being caused by a respiratory virus, pollution or allergies.[44,45] According to the common sense model of illness, such beliefs can have an impact on a variety of illness outcomes.[46] Research has shown that external causal attributions are associated with adherence to asthma medication; however, it is unclear whether these beliefs are associated with higher or lower levels of adherence.[47,48] The impact of causal attributions on illness outcome has not yet been explored in relation to other types of asthma treatment such as breathing retraining. The Brief IPQ item asks people to write their own top three (in rank order) perceived causes of their illness; therefore, we did not need to use or create a list. However, as the most common items selected by people with asthma are hereditary, a respiratory virus, pollution and allergies, we expected these to be the main responses to this question.
- *Perceived chronicity*. A single item was used to measure whether or not participants believed that asthma was a chronic condition.[49] Many people with asthma perceive their illness to be an acute episodic illness rather than a chronic one. The belief that they have asthma only if they are having symptoms (the 'no symptoms, no asthma' belief) is associated with low adherence to inhaled corticosteroids and beliefs that inhaled corticosteroids are important to use when symptomatic but not asymptomatic, and with lower participation in self-management tasks such as peak flow monitoring or routine doctor visits.[49]

First impressions of the treatment

- *Expectancy*. Expectancy (improvements that a person believes will be personally achieved during treatment)[50] is an important non-specific factor that can impact on the adherence to and outcome of treatment.[51] As well as being an important non-specific factor, outcome expectancy (along with self-efficacy) is also a central tenet of Bandura's social cognitive theory.[52] It was expected that the face-to-face treatment group would reach greater levels of expectancy than the home-based treatment group. Expectancy was measured using the three expectancy items from the Credibility/Expectancy Questionnaire,[50] which were standardised and summed for analysis.
- *Self-efficacy*. Self-efficacy is a well-documented predictor of treatment outcome and, together with expectancy, has been associated with subjective recovery and adherence to physiotherapy[53] and outcomes such as AQLQ score in people with asthma.[54,55] The items selected were based on Lorig's three-item Exercise Regularly Scale,[56] which was created to assess self-efficacy to perform self-management behaviours in people with chronic disease, correctly, every day and without making their symptoms worse. The three self-efficacy items are rated on a scale from 0 to10. Responses were summed and averaged for analysis.
- *Perceived need for support (baseline)*. A single-item question was included to assess how important the participants (in both active treatment groups) felt it would be to receive physiotherapist support (i.e. whether the physiotherapist sessions were anticipated by participants to be useful and adding value beyond the booklet itself, regardless of whether or not they would be receiving this support).
- *Theory of planned behaviour*. The theory of planned behaviour model hypothesises that attitudes, subjective norms and perceived behavioural control will predict intentions and that intentions and perceived behavioural control will predict behaviour (engagement and amount of practice). Consistent with guidance on constructing a theory of planned behaviour questionnaire,[57] semistructured

qualitative interviews were conducted to elicit salient beliefs to create appropriate items relating to the components of the model.[37] Items in each subscale were summed to create a composite score for analysis. The factor structure of the constructs was checked using exploratory factor analysis, with principal axis factoring and direct oblimin rotation, and internal reliability was checked using Cronbach's alpha. The structure and internal reliability of the constructs were suitable for further analysis, with the exception of control-related beliefs, which were of borderline acceptability ($\alpha = 0.69$). Therefore, the two items in the control-related beliefs construct were used separately as single items in further analyses. Redundancy (indicated by multicollinearity) were also noted within the attitudes, subjective norms and intentions constructs. Although the constructs were summed for these analyses, future work could reduce participant burden by using a single item for each of these constructs.

- Attitudes – three items were created to assess the belief that carrying out the intervention would be good/bad, beneficial/harmful or useful/useless. Items were reverse coded so that higher scores reflected a more positive attitude. The internal reliability of the construct was excellent ($\alpha = 0.94$).
- Subjective norms – three items were created to assess the perception that important others believed that carrying out the intervention would be good/bad, beneficial/harmful or useful/useless. Items were reverse coded so that higher scores reflected a more positive view ($\alpha = 0.98$).
- Perceived behavioural control – two items were created to assess the perception that it would be possible to carry out the intervention and that participants were confident that they could carry out the intervention ($\alpha = 0.89$).
- Intentions – intentions were assessed by three items measuring whether participants would try to, intended to and wanted to carry out the intervention ($\alpha = 0.96$). Because of a ceiling effect ($n = 168$, 44% of participants endorsing the maximum scores), the data were recoded into a binary variable (high = 21/low < 21).
- Beliefs (attitude related) – four items were created to assess whether the intervention would be relevant, reduce the use of a reliever inhaler, help the patient to feel more in control of asthma and help the patient to feel more relaxed ($\alpha = 0.87$).
- Beliefs (control related) – two items were created to assess whether the intervention was perceived to be time-consuming and difficult to fit into the daily routine. These were used in the analysis as single items.

Treatment experience (3 months' follow-up)

- *Enjoyment*. Intrinsic motivation is an important factor in adherence to rehabilitation and exercise.[58,59] Enjoyment is a factor that is considered to underlie intrinsic motivation.[60,61] Given the different aspects of the trial intervention, it was expected that participants would enjoy the therapist appointments, relaxation and controlled breathing, but dislike the controlled breath holding. It was unclear whether they would enjoy or dislike carrying out additional physical exercise/activity. The single item measuring enjoyment used by Reeve,[60] with responses measured on a scale from 0 to 10, ranging from not at all enjoyable to extremely enjoyable, was selected for this study. To allow for the expectation that some might find the controlled breath holding aversive (a stronger response than not enjoyable), the scale was adapted from extremely enjoyable to not at all enjoyable to extremely enjoyable to extremely unpleasant. This question wording presents less bias, allowing a non-judgemental basis for participants to provide more honest answers. The question was repeated six times in relation to the different aspects of the intervention (stomach breathing, nose breathing, slow breathing, controlled breath holding, relaxation training and, in the physiotherapy group only, appointments with the physiotherapist).
- *Perceived need for support*. A single-item question was included to assess change since baseline in how important the participants (in both the DVD group and the physiotherapy group) perceived the physiotherapist support to be (i.e. whether the physiotherapist sessions were perceived by participants to be useful and to add value beyond the booklet itself, regardless of whether they received this support or not).
- *Perceptions of the physiotherapist (physiotherapy group only)*. The Treatment Appraisal Questionnaire[62] contains five single items (measured on a scale from 1 to 7) relating to 'perceptions of the therapist'.

The items assess the degree of trust in the therapist, confidence in the therapist's qualifications and competence and the extent to which participants feel comfortable talking to the therapist about their health and believe that the therapist wants to help them. These factors may all be relevant to participants undergoing face-to-face treatment. Because of a ceiling effect ($n = 74$, 77% of participants endorsing the maximum score), the data were recoded into a binary variable (high = 35/low < 35).

- *Problematic Experiences of Therapy Scale*. Participants' perceptions of any adherence problems were measured using the PETS.[43] The PETS was developed to measure patient perceptions of barriers to adherence to home-based rehabilitation. The four validated PETS subscales were included (problems due to symptoms – three items; problems due to uncertainty about the therapy – three items; problems due to doubts – three items; and practical problems – five items), along with a new theoretically derived subscale to measure problems due to lack of support (three items).
- *Treatment engagement*. A range of items was included to measure participants' level of engagement with breathing retraining in terms of how much they carried out breathing retraining and which techniques they used. The following items were included:

    - Carrying out the breathing retraining:

        - Number of weeks that the breathing retraining was carried out for.
        - Days per week on average that the breathing retraining was carried out for.
        - Times per day on average that the breathing retraining was carried out for.
        - Engagement – engagement is a composite binary variable in which 'engaged' was defined as giving any response above 'never started' to any of the first three questions above (number of weeks, days per week and times per day). Participants were defined as non-engaged if they did not start breathing retraining at all.
        - Reason for stopping regular breathing retraining (because they no longer have symptoms of asthma or for other reasons).
        - Continuation with occasional breathing retraining (despite not carrying out regular breathing retraining) – specified in relation to as many as applied out of stomach breathing, nose breathing, slow breathing, controlled breath holding or relaxation training.

    - Total time spent on each type of technique:

        - stomach breathing (number of weeks/hours per day)
        - nose breathing (number of weeks/hours per day)
        - slow breathing (number of weeks/minutes per day)
        - controlled breath holding (number of weeks/minutes per day)
        - relaxation training (number of weeks/minutes per day).

    - Amount of practice – amount of practice is a continuous variable that was calculated by multiplying the responses to the first three questions within the 'Carrying out the breathing retraining' section. These questions related to the number of weeks, number of days per week and number of times per day, on average, that the breathing retraining was carried out. Participants who did not engage with the breathing retraining were excluded from the analyses.

Continued treatment engagement (6 and 12 months' follow-up)

- Five items were included to measure whether participants had continued to carry out breathing retraining at 6 and 12 months. The five items consisted of one question for each technique (stomach breathing, nose breathing, slow breathing, controlled breath holding and relaxation training) to find out how often participants had carried out the exercises [measured on a five-point scale ranging from never to regularly (most days)].

Results

Sensitivity analyses for engagement with and amount of practice of breathing exercises reported at 3 months' follow-up

These are reported with the main trial results (see *Chapter 3*, *Patient engagement with the intervention in the active treatment arms*.)

Analyses of between-group differences to explore whether there is a difference between the two intervention groups on measures of expectancy, experience, treatment engagement and practical barriers

T-tests and chi-squared tests were used to explore whether there were any differences between the treatment groups on measures of expectancy, experience, treatment engagement and practical barriers. Content analysis was performed on the three open-ended text items that measured perceived causes. A total of 937 responses were given, the majority of which could be grouped into eight main themes: allergies (245 responses), health issues (142 responses, such as viral infections, radiotherapy, obesity, pregnancy/menopause, glandular fever and childhood conditions), smoking (114 responses), pollution/environmental causes (104 responses), hereditary causes (79 responses), stress/psychological causes (65 responses), weather (65 responses) and exercise (59 responses). The three categories with the highest frequencies (allergy, health issues and smoking) were binary coded into present/absent in the data and used in between-group analyses. Participants could attribute up to three causes. Using this recoded data, a total of 192 participants (49%) believed that their asthma was caused by allergies, 120 (31%) by health issues and 110 (28%) by smoking.

With regard to perceived chronicity, 44% of participants thought of asthma as a chronic disease, with the remainder reporting some degree of the 'no symptoms, no asthma', acute episodic disease belief (16% believed that they had asthma most of the time, 20% some of the time and 21% only when they were having symptoms). The data were analysed in relation to each of these four categories separately.

There were no significant differences between the two treatment arms with regard to beliefs about the causes or chronicity of asthma. However, having been given the booklet to look through and told what group they had been allocated to, the face-to-face physiotherapy group had more positive perceptions of breathing retraining than the DVD group. (*Table 49*). Being aware that they would be receiving physiotherapist support led to significantly more positive attitudes and attitude-related beliefs, a greater sense of perceived behavioural control and higher intentions to carry out breathing retraining in the physiotherapy group. Those anticipating physiotherapist support were significantly less likely to believe that carrying out breathing retraining would be too time-consuming or difficult to fit into their daily routine. Those who were aware that they had been randomised to the physiotherapist group felt a significantly greater need for the physiotherapist support than those who were aware that they had been randomised to the DVD group.

The majority of participants in the face-to-face physiotherapy group found the appointments with the physiotherapist to be extremely enjoyable (93% rated the appointments as ≥ 8 out of 10) and 77% had the best possible perceptions of their physiotherapist. Those in the face-to-face physiotherapy group continued to perceive a significantly greater need for physiotherapist support than those in the DVD group and they also reported a significantly more positive treatment experience in relation to enjoyment of stomach breathing, nose breathing and relaxation training than those in the DVD group. They also experienced significantly fewer problems as a result of symptoms, uncertainty, doubt and lack of support. There were no differences between the face-to-face physiotherapy group and the DVD group in terms of the level of enjoyment of controlled breath holding or practical problems (*Table 50*).

Overall, engagement with breathing retraining was extremely high, with 98.1% of responders reporting that they had attempted at least one of the breathing retraining techniques (*Table 51*). Only five participants (1.9%), who were all allocated to the DVD group, reported not attempting any breathing retraining at all. Participants who had received face-to-face physiotherapy were significantly more likely than those in the DVD group to have carried out breathing retraining more times per day, more days per week and for more

TABLE 49 Beliefs about asthma and first impressions of the treatment in the face-to-face physiotherapy and DVD arms

Beliefs about asthma and first impressions of treatment	Treatment arm, baseline		Group difference[a]	*p*-value
	DVD	Physiotherapy		
Beliefs about asthma,* n *(%)				
Perceived causes				
Cause 1 – allergy	125 (48)	67 (51)	0.29	0.592
Cause 2 – health issues	81 (31)	39 (30)	0.09	0.762
Cause 3 – smoking	69 (26)	41 (31)	0.93	0.335
Perceived chronicity			2.03	0.566
All the time	112 (45)	54 (42)		
Most of the time	41 (16)	18 (14)		
Some of the time	45 (18)	31 (24)		
Only when symptoms present	52 (21)	27 (21)		
First impressions of treatment, mean (SD)[b]				
Expectancy ($n = 243$, $n = 124$)	–0.11 (2.74)	0.24 (2.66)	–1.20 (–0.95 to 0.23)	0.233
Self-efficacy ($n = 252$, $n = 129$)[c]	7.70 (1.62)	8.01 (1.48)	–1.84 (–0.62 to 0.05)	0.067
Perceived need for physiotherapist support – baseline ($n = 250$, $n = 127$)[c]	2.15 (1.26)	3.43 (0.87)	–11.48 (–1.49 to –1.06)	0. 001
Theory of planned behaviour constructs				
Attitudes ($n = 239$, $n = 119$)[c]	16.45 (3.75)	17.74 (2.82)	–3.64 (–1.96 to –0.66)	0.001
Subjective norms ($n = 235$, $n = 117$)[c]	16.82 (3.89)	17.62 (3.72)	–1.85 (–1.62 to –0.04)	0.059
Perceived behavioural control ($n = 251$, $n = 130$)[c]	11.05 (2.64)	12.07 (2.37)	–3.84 (–1.56 to –0.47)	0.001
Intentions, *n* (%) ($n = 249$, $n = 129$)	99 (40)	69 (54)	6.49	0.011
Beliefs (attitude related) ($n = 245$, $n = 125$)[c]	21.99 (4.23)	23.07 (4.37)	–2.31 (–1.98 to –0.19)	0.020
Beliefs (control related)				
Time-consuming ($n = 252$, $n = 127$)[c]	4.10 (1.80)	3.65 (1.73)	–2.31 (0.03 to 0.83)	0.024
Difficult to fit into routine ($n = 252$, $n = 126$)[c]	3.33 (1.74)	2.86 (1.73)	–2.47 (0.08 to 0.86)	0.013

a For categorical variables [baseline scores presented as *n* (%)] chi-squared test statistics are presented; for continuous variables [baseline scores presented as mean (SD)] parametric *t*-test statistics and 95% CIs are presented (bootstrapped when specified).
b *n* values represent numbers of included participants in the DVD and physiotherapy groups respectively.
c Bootstrapped 95% CI and *p*-value reported.

weeks, and to have completed more practice sessions. This particularly applied to the stomach breathing and nose breathing, but also to the slow breathing and controlled breath holds to a lesser, but still significant, extent. Among those who stopped regular practice ($n = 97$), those in the face-to-face physiotherapy group were significantly more likely to continue with occasional practice of nose breathing.

The positive effect of physiotherapist support on stomach breathing and nose breathing also had lasting effects, with participants in the physiotherapy group continuing to carry out the stomach breathing and nose breathing significantly more often than those in the DVD group at both 6 months' and 12 months' follow-up (*Table 52*).

TABLE 50 Perceived experience of carrying out breathing retraining in the face-to-face physiotherapy and DVD arms

Treatment experience[a]	Treatment arm, 3-month follow-up		Group difference[b]	*p*-value
	DVD	Physiotherapy		
Enjoyment of treatment, mean (SD)				
Stomach breathing ($n = 159$, $n = 104$)	6.13 (1.99)	7.42 (1.67)	–5.71 (–1.75 to –0.85)	< 0.001
Nose breathing ($n = 160$, $n = 104$)	6.06 (2.18)	7.52 (1.78)	–5.96 (–1.95 to –0.98)	< 0.001
Slow breathing ($n = 159$, $n = 103$)	6.22 (2.01)	6.69 (2.12)	–1.81 (–0.98 to 0.04)	0.072
Controlled breath holding ($n = 158$, $n = 103$)	5.54 (2.29)	5.43 (2.18)	0.41 (–0.44 to 0.68)	0.681
Relaxation training ($n = 155$, $n = 102$)	6.97 (1.80)	7.62 (2.38)	–2.32 (–1.19 to –0.10)	0.022
Appointments with physiotherapist (physiotherapy group only) ($n = 103$), median (IQR); minimum, maximum		9 (9–10); 1, 10		
Perceived need for physiotherapist support (3 months) ($n = 158$, $n = 101$), mean (SD)	1.85 (1.38)	3.64 (0.72)	–13.73 (–2.05 to –1.54)	< 0.001
Perceptions of physiotherapist (physiotherapy group only) ($n = 96$), *n* (%)		74 (77)		
PETS, *n* (%)				
Problems due to symptoms ($n = 155$, $n = 103$)	49 (31.6)	21 (20.4)	3.94	0.047
Problems due to uncertainty ($n = 156$, $n = 101$)	75 (48.1)	14 (13.9)	31.71	< 0.001
Problems due to doubts ($n = 166$, $n = 105$)	90 (54.2)	24 (22.9)	25.95	< 0.001
Practical problems ($n = 166$, $n = 105$)	141 (84.9)	84 (80.0)	1.11	0.291
Problems due to lack of support ($n = 166$, $n = 105$)	74 (44.6)	17 (16.2)	23.24	< 0.001

a *n* values represent numbers of included participants in the DVD and physiotherapy groups respectively.
b Unless specified otherwise, for categorical variables [baseline scores presented as *n* (%)] chi-squared test statistics are presented; for continuous variables [baseline scores presented as mean (SD)] parametric *t*-test statistics and 95% CIs are presented.

TABLE 51 Engagement and number of practice sessions completed in the face-to-face physiotherapy and DVD arms

Engagement and number of practice sessions[a]	Treatment arm, 3-month follow-up		Group difference[b]	*p*-value
	DVD	Physiotherapy		
Carrying out the breathing retraining				
Engagement with breathing retraining (overall) ($n = 261$, $n = 132$), *n* (%)	256 (98.1)	132 (100)	2.56	0.110
Number of weeks[c,d] ($n = 165$, $n = 103$), mean (SD)	3.68 (1.38)	4.32 (0.87)	–4.67 (–0.92 to –0.38)	0.001
Days per week[c,e] ($n = 165$, $n = 103$), mean (SD)	2.52 (1.20)	3.08 (1.02)	4.07 (–0.83 to –0.28)	0.001
At least twice per day ($n = 164$, $n = 105$), *n* (%)	46 (28.0)	58 (55.2)	19.96	< 0.001
Amount of practice sessions completed (overall)[c] ($n = 164$, $n = 102$), mean (SD)	48.56 (44.71)	75.01 (46.38)	–26.45 (–37.68 to –14.97)	0.001
Stopped regular practice as no asthma symptoms ($n = 162$, $n = 105$), *n* (%)	14 (8.6)	5 (4.8)	1.45	0.228
Stopped regular practice for other reasons ($n = 160$, $n = 101$), *n* (%)	61 (38.1)	27 (26.7)	3.60	0.058

TABLE 51 Engagement and number of practice sessions completed in the face-to-face physiotherapy and DVD arms (*continued*)

Engagement and number of practice sessions[a]	Treatment arm, 3-month follow-up		Group difference[b]	*p*-value
	DVD	Physiotherapy		
Stopped regular practice but continued with occasional practice, *n* (%)				
Overall (*n* = 66, *n* = 31)	61 (92.4)	30 (96.8)	0.69	0.407
Stomach breathing (*n* = 61, *n* = 30)	44 (72.1)	26 (86.7)	2.39	0.122
Nose breathing (*n* = 61, *n* = 30)	38 (62.3)	26 (86.7)	5.72	0.017
Slow breathing (*n* = 61, *n* = 30)	42 (68.9)	19 (63.3)	0.28	0.599
Controlled breath holding (*n* = 61, *n* = 30)	13 (21.3)	6 (20.0)	0.02	0.885
Relaxation training (*n* = 61, *n* = 30)	27 (44.3)	10 (33.3)	1.00	0.318
Total time spent on each breathing technique, mean (SD)				
Stomach breathing				
Number of weeks[d] (*n* = 159, *n* = 100)	3.53 (1.56)	4.35 (1.05)	–5.03 (–1.16 to –0.49)	0.001
Hours per day[f] (*n* = 157, *n* = 99)	1.39 (0.99)	2.11 (1.20)	–5.00 (–1.01 to –0.42)	0.001
Nose breathing				
Number of weeks[d] (*n* = 159, *n* = 101)	3.52 (1.66)	4.33 (1.03)	–4.81 (–1.14 to –0.47)	0.001
Hours per day[f] (*n* = 157, *n* = 101)	1.81 (1.27)	2.45 (1.34)	–3.81 (–0.97 to –0.34)	0.001
Slow breathing				
Number of weeks[d] (*n* = 160, *n* = 101)	3.44 (1.53)	3.89 (1.27)	–2.55 (–0.80 to –0.11)	0.012
Minutes per day[g] (*n* = 159, *n* = 101)	2.10 (1.35)	2.45 (1.28)	–2.05 (–0.68 to –0.02)	0.039
Controlled breath holding				
Number of weeks[d] (*n* = 160, *n* = 101)	2.88 (1.76)	3.32 (1.57)	–2.08 (–0.79 to –0.07)	0.020
Minutes per day[h] (*n* = 159, *n* = 101)	1.74 (1.09)	1.83 (1.11)	–0.69 (–0.37 to 0.19)	0.497
Relaxation training				
Number of weeks[d] (*n* = 160, *n* = 101)	3.01 (1.86)	3.29 (1.66)	–1.27 (–0.70 to 0.16)	0.217
Minutes per day[i] (*n* = 160, *n* = 101)	1.86 (1.24)	1.64 (1.20)	1.41 (–0.10 to 0.50)	0.159

a *n* values represent numbers of included participants in the DVD and physiotherapy groups respectively.
b For categorical variables [baseline scores presented as *n* (%)] chi-squared test statistics are presented; for continuous variables [baseline scores presented as mean (SD)] parametric *t*-test statistics and 95% CIs are presented (bootstrapped when specified).
c Bootstrapped 95% CIs and *p*-values reported.
d Coding: 0 = did not use, 1 = 1 week, 2 = 1–2 weeks, 3 = 3–5 weeks, 4 = 6–8 weeks, 5 = ≥ 9 weeks.
e Coding: 0 = did not use, 1 = 1–2 days, 2 = 3–4 days, 3 = 5–6 days, 4 = most days.
f Coding: 0 = did not use, 1 = ≤ 1 hour, 2 = ≤ half a day, 3 = > half a day, 4 = most of the day.
g Coding: 0 = did not use, 1 = up to 5 minutes, 2 = 6–10 minutes, 3 = 11–20 minutes, 4 = 21–30 minutes, 5 = ≥ 30 minutes.
h Coding: 0 = did not use, 1 = up to 2 minutes, 2 = 3–5 minutes, 3 = 6–8 minutes, 4 = ≥ 8 minutes.
i Coding: 0 = did not use, 1 = up to 5 minutes, 2 = 6–10 minutes, 3 = 11–15 minutes, 4 = ≥ 15 minutes.

Correlates and predictors of the amount of practice and continued engagement

Analyses were carried out to assess whether expectancy, experience and practical barriers were associated with amount of practice (at 3 months) and continued engagement (at 6 months and 12 months). As engagement was 98% in the DVD group and 100% in the face-to-face physiotherapy group, there was no variation in the data to be able to carry out the planned analyses in relation to non-engagement.

TABLE 52 Continued engagement at 6 and 12 months in the face-to-face physiotherapy and DVD arms

Exercise[a]	Treatment arm, mean (SD)		Group difference[b]	*p*-value
	DVD	Physiotherapy		
6-month follow-up				
Number included	156	96		
Stomach breathing	2.18 (1.24)	2.94 (1.02)	–5.04 (–1.05 to –0.46)	< 0.001
Nose breathing	2.43 (1.31)	2.83 (1.19)	–2.46 (–0.73 to –0.08)	0.014
Slow breathing	2.22 (1.20)	2.48 (1.11)	–1.73 (–0.56 to 0.36)	0.085
Controlled breath holding	1.92 (1.26)	1.81 (1.16)	0.70 (–0.20 to 0.42)	0.512
Relaxation training	1.83 (1.24)	2.01 (1.30)	–1.12 (–0.51 to 0.14)	0.264
12-month follow-up				
Number included	153	96		
Stomach breathing	2.18 (1.18)	2.72 (1.12)	–3.59 (–0.84 to –0.25)	< 0.001
Nose breathing	2.31 (1.25)	2.66 (1.26)	–2.09 (–0.67 to –0.02)	0.037
Slow breathing	2.20 (1.17)	2.38 (1.07)	–1.21 (–0.47 to 0.11)	0.226
Controlled breath holding	1.84 (1.20)	1.66 (1.03)	1.22 (–0.11 to 0.47)	0.225
Relaxation training	1.75 (1.22)	1.93 (1.19)	–1.16 (–0.49 to 0.13)	0.249

a Coding: 0 = never, 1 = once or twice, 2 = sometimes, 3 = often, 4 = regularly (most days).
b Parametric *t*-test statistics and 95% CIs are presented (bootstrapped when specified).

For the continuous outcomes (amount of practice at 3 months and continued engagement at 6 months and 12 months), point-biserial (for binary expectancy variables) and bivariate (for continuous expectancy variables, treatment experience and practical barriers) correlations were used to identify significant variables to be entered into multiple linear regressions for each outcome. All of the correlations are presented in *Appendix 13* and significant correlations are presented in *Table 53*.

Among the correlations, a moderate-sized effect size was found for the relationship between self-efficacy and amount of practice at 3 months and continued engagement at both 6 and 12 months, but only in the DVD group. Believing that asthma was caused by allergy was associated with more practice at 3 months in the face-to-face physiotherapy group. Believing that asthma was caused by health issues was associated with less continued engagement at 12 months in the DVD group. Believing that asthma was caused by smoking was associated with both more practice at 3 months in the DVD group and greater continued engagement at 12 months in the face-to-face physiotherapy group.

In the DVD group, higher expectancy (agreeing strongly that asthma symptoms will be improved by breathing retraining), greater self-efficacy for breathing retraining and greater perceived behavioural control regarding breathing retraining were associated with more practice at 3 months and greater continued engagement at 6 months. However, the only one of these factors that predicted greater continued engagement at 12 months was self-efficacy for breathing retraining. In addition, stronger intentions to carry out breathing retraining were associated with greater continued engagement at 6 and 12 months in the DVD group. Although the perceived need for support was high in the face-to-face physiotherapy group at baseline, it did not relate to the amount of practice or continued engagement.

In the DVD group, greater enjoyment of treatment was associated with more practice at 3 months and greater continued engagement at 6 and 12 months for all aspects of breathing retraining (stomach breathing, nose breathing, slow breathing, controlled breath holds and relaxation). However, the findings were less

TABLE 53 Expectancy, experience and practical barriers variables that were significantly correlated with amount of practice (at 3 months) and continued engagement (at 6 and 12 months)

Amount of practice at 3 months		Continued engagement at			
		6 months		12 months	
DVD	Physiotherapy	DVD	Physiotherapy	DVD	Physiotherapy
• Cause: smoking • Asthma present 'most of the time' • Expectancy • Self-efficacy • Perceived behavioural control • Stomach breathing • Nose breathing • Slow breathing • Controlled breath holding • Relaxation training • Perceived need for support (3 months) • Problems due to uncertainty • Problems due to doubts • Practical problems • Problems due to lack of support	• Cause: allergy • Stomach breathing • Nose breathing • Perceived need for support (3 months) • Perceptions of physiotherapist • Problems due to doubts • Practical problems • Problems due to lack of support	• Expectancy • Self-efficacy • Perceived behavioural control • Intentions • Stomach breathing • Nose breathing • Slow breathing • Controlled breath holding • Relaxation training • Problems due to symptoms • Problems due to uncertainty • Problems due to doubts • Practical problems • Problems due to lack of support	• Stomach breathing • Nose breathing • Controlled breath holding • Relaxation training	• Cause: health issues • Self-efficacy • Intentions • Stomach breathing • Nose breathing • Slow breathing • Controlled breath holding • Relaxation training • Problems due to doubts • Practical problems • Problems due to lack of support	• Cause: smoking • Stomach breathing • Slow breathing • Controlled breath holding • Relaxation training • Perceived need for support (3 months)

consistent for the face-to-face physiotherapy group. Greater enjoyment of treatment was associated with more practice at 3 months for stomach and nose breathing, greater continued engagement at 6 months for stomach breathing, nose breathing, controlled breath holding and relaxation and greater continued engagement at 12 months for stomach breathing, slow breathing, controlled breath holding and relaxation. Experience of appointments with the physiotherapist was not related to practice or continued engagement.

With regard to practical barriers, in the DVD group problems due to uncertainty were associated with less practice at 3 months and less continued engagement at 6 months. Problems due to doubts, practical problems and lack of support were associated with less practice at 3 months in both the DVD group and the face-to-face physiotherapy group. Problems due to doubts and practical problems were associated with less continued engagement at 6 and 12 months in the DVD group only. Problems due to lack of support were associated with less continued engagement at 6 months in the DVD group only. Problems due to symptoms were associated with less continued engagement at 6 months in the DVD group only.

The significant correlates shown in *Table 53* were input into the multiple regression detailed in *Appendix 14* to predict the amount of practice at 3 months. More practice at 3 months was predicted by fewer practical problems and fewer problems due to lack of support (R2 = 0.33, ($F_{17,66} = 1.92$; $p < 0.05$). This model explained 33% of the variance in practice at 3 months. This means that individuals who experienced fewer practical problems in carrying out breathing retraining and fewer problems due to lack of support practised more.

The significant correlates shown in *Table 53* were input into the multiple regression detailed in *Appendix 15* to predict continued engagement at 6 months. More engagement at 6 months was predicted by fewer problems due to symptoms, fewer problems due to doubts and finding relaxation training enjoyable. This model explained 24% of the variance in continued engagement at 6 months ($F_{14,174} = 3.97$; $p < 0.001$). According to this model, individuals who experienced fewer problems due to symptoms and doubts and who found relaxation training more enjoyable were more likely to continue to engage with breathing training at 6 months.

The significant correlates shown in *Table 53* were input into the multiple regression in *Appendix 16* to predict variables associated with continued engagement at 12 months. The overall model was significant, explaining 17% of the variance in continued engagement at 12 months ($F_{12,173} = 3.05$; $p < 0.001$). However, no individual predictors of continued engagement at 12 months were identified.

Analyses to model the theory of planned behaviour and explore whether intentions, amount of practice, engagement and continued engagement can be predicted by the model

The theory of planned behaviour hypothesises that attitudes, subjective norms and perceived behavioural control will predict intentions and that intentions and perceived behavioural control will predict behaviour (amount of practice and continued engagement at 6 months and 12 months). Correlational analyses indicated that there is a strong relationship among most of the variables (see *Appendix 17*).

A logistic regression was carried out to assess the role of attitudes, subjective norms and perceived behavioural control in the prediction of intentions (see *Appendix 18*). Overall, the model was a good fit to the data (χ^2 (6) = 154.23; $p < 0.001$). Perceived behavioural control was found to be a significant predictor of intentions (odds ratio 2.21, 95% CI 1.79 to 2.72), but attitudes and subjective norms were not.

A hierarchical linear regression assessed the role of intentions and perceived behavioural control in predicting continued engagement at 6 months (see *Appendix 19*). The final model, in which perceived behavioural control was the only significant predictor of continued engagement, explained 3% of the variance in continued engagement at 6 months: ($F_{2,242} = 7.31$; $p < 0.001$).

A multiple regression was carried out to assess the role of intentions and perceived behavioural control in predicting continued engagement at 12 months (see *Appendix 20*). Intention was entered in the first step and was a significant predictor (95% CI 0.40 to 2.71). Although neither factor was significant at the second step, the model was a significant predictor, explaining 3% of the variance ($F_{2,238} = 3.87$; $p < 0.05$).

Finally, a multiple regression was carried out to assess the role of intentions and perceived behavioural control in predicting the amount of practice at 3 months (see *Appendix 21*). No significant predictors were identified. The model explained 1% of the variance in the amount of practice at 3 months ($F_{2,257} = 2.99$; $p = 0.05$).

Checking the factor structure of the Problematic Experiences of Therapy Scale

The factor structure of the PETS was checked using exploratory factor analysis [principal axis factoring, with oblique (direct oblimin) rotation to allow for correlations between factors] as (1) it has not previously been used in an asthma population and (2) the 'problems due to lack of support' subscale questions were new and had not previously been validated. The model was forced into the hypothesised five-factor solution and items 3 and 5 were excluded from the analysis because of multicollinearity. The fit of the final model was good. The determinant (0.00002) indicated no further multicollinearity and the Kaiser–Meyer–Olkin (KMO) measure of sampling adequacy indicated that the data were suitable for factor analysis (KMO = 0.86). Bartlett's test of sphericity was significant (χ^2 (105) = 2283.81; $p < 0.001$), indicating that there was a sufficient relationship between the variables. Communalities were all > 0.5, indicating sufficient common variance between the variables. The pattern matrix (see *Appendix 22*) showed that all items loaded clearly onto their intended factors (all loadings were > 0.63, with no cross-loading). The biggest amount of variance in the data set was explained by the new 'problems due to lack of support' subscale, which accounted for 44.49% of the total variance, substantially more than any of the other subscales (which ranged between 6.64% and 15.25%).

All subscales showed good internal consistency. The inter-item correlation matrices were all > 0.3 and the corrected item–total correlations were also well above 0.3. The overall Cronbach's alpha values were all good and ranged from 0.76 to 0.90 (see *Appendix 22*). A higher Cronbach's alpha value (increasing from 0.85 to 0.90) could have been achieved if item 15 were deleted from the 'problems due to lack of support' subscale. However, it was decided to retain the item as it had a good theoretical fit and seemed suitable according to all other aspects of the exploratory factor and Cronbach's alpha analyses. *Appendix 23* shows the component correlation matrix between the five factors. It is interesting to note that there are both positive and negative relationships between the factors.

Discussion

After being informed of group allocation, the face-to-face physiotherapy group had more positive perceptions of breathing retraining than the DVD group, including greater intentions to carry out the exercises and being less likely to believe that carrying out breathing retraining would be too time-consuming or difficult to fit into their daily routine. This suggests that physiotherapy delivered by a physiotherapist may be more positively received than a DVD, and health-care professionals need to think of ways to enhance the appeal of breathing retraining delivered by DVD in practice. Those who were aware that they had been randomised to the physiotherapist group also felt a significantly greater need for physiotherapist support than those who were aware that they had been randomised to the DVD group. This suggests that the anticipation of support can raise expectations about how much that support is needed. This should be taken into account when considering patient expectation management in clinical practice. This is particularly important as the face-to-face physiotherapy group continued to perceive a need for physiotherapist support.

The face-to-face physiotherapy group found the appointments with the physiotherapist to be extremely enjoyable and reported greater enjoyment of the stomach breathing, nose breathing and relaxation exercises than those in the DVD group. They also experienced significantly fewer problems due to symptoms, uncertainty, doubt and lack of support. This shows that the participants in the face-to-face physiotherapy group felt supported by the physiotherapist and suggests that seeing a physiotherapist is the

ideal treatment for maximising enjoyment of breathing retraining. However, as the trial was carried out by a single physiotherapist, it is not clear whether these findings were the result of individual factors related to the physiotherapist or simply the act of seeing a physiotherapist. Further research is needed to explore experiences of breathing retraining carried out by more than one physiotherapist. Overall, levels of engagement with breathing retraining were extremely high, suggesting that access to a DVD plus the *Breathing Freely* booklet is sufficient for enabling engagement.

Those in the face-to-face physiotherapy group also spent significantly more time practising breathing retraining and were more likely to continue to carry out the stomach breathing and nose breathing exercises at 6 and 12 months than those in the DVD group. This may be because their initial greater levels of practice led to stomach and nose breathing becoming new habits, in line with research that habit formation is an effective behaviour change strategy.[41]

A moderate effect size was found for the relationship between self-efficacy and amount of practice at 3 months and continued engagement at both 6 and 12 months, but only in the DVD group. This suggests that if people with asthma are being expected to undertake breathing retraining with just the support of a DVD, it is important that they are confident that they can carry out breathing retraining correctly every day and without making their symptoms worse. However, although the perceived need for support was high in the face-to-face physiotherapy group at baseline, it did not relate to the amount of practice or continued engagement.

Believing asthma to be caused by health issues was associated with less continued engagement at 12 months in the DVD group. This is in line with the medical model: if people believe that asthma is not under their control, they may be less likely to engage with interventions to reduce symptoms.

In the DVD group, greater enjoyment of treatment was associated with more practice at 3 months and greater continued engagement at 6 and 12 months, for all aspects of breathing retraining. This suggests that if people with asthma are being expected to undertake breathing retraining delivered by DVD, it may be helpful to maximise enjoyment by presenting it in an attractive way. However, these findings were less consistent for those in the face-to-face physiotherapy group, maybe because seeing the physiotherapist provided them with greater extrinsic motivation to practise initially.

In the DVD group, more problems due to uncertainty, doubts, practical problems and lack of support were associated with less practice at 3 months and less continued engagement. This suggests that, if people with asthma are not confident about breathing retraining and do not feel supported in carrying it out, they may experience problems in engaging with it. Future research could examine whether or not this issue might be addressed by providing some (e.g. telephone or online) access to physiotherapist support.

Conclusions

Implications for health care and recommendations for research

Almost all participants engaged with breathing retraining, suggesting that it is likely to be valued as a method of asthma management. Participants in the face-to-face physiotherapy group enjoyed the techniques more, reported practising more at 3 months and demonstrated greater continued engagement at 6 and 12 months, but this was not associated with better outcomes. In the DVD group, those who enjoyed the techniques more and reported greater confidence in their ability to carry them out also practised more at 3 months and demonstrated greater continued engagement with the techniques at 6 and 12 months.

Chapter 7 Discussion

Study findings

Overview

We report the results of a pragmatic, three-arm, parallel-group RCT comparing the effectiveness of a breathing retraining programme for people with suboptimal asthma control delivered by a self-guided programme (as a DVD with a supporting booklet, both developed for the study) with the effectiveness of a three-session face-to-face breathing retraining programme delivered by a respiratory physiotherapist and a control consisting of usual care. To our knowledge this is by far the largest and most rigorous study on breathing retraining exercise to be reported in the world literature. This was designed as a 'pragmatic' study, that is, one that had broad entry criteria to allow the participation of most people with asthma in the community and that included study measurements and procedures that interfered as little as possible with usual clinical care. Only two study-related visits were made (at baseline and 12 months), with two further postal questionnaires at 3 and 6 months, and normal care was allowed to proceed over the 12 months of the study. We supplemented visit measurements and questionnaire data with routinely collected clinical data from the GP medical record. Our primary outcome was asthma-related QoL, with measurement of a range of other patient-reported outcomes, objective physiological outcomes and health resource use outcomes. A formal health economic evaluation was built into the programme and both qualitative and quantitative process evaluations were carried out. The study was set in primary care, recruiting from research general practices in Wessex through the CRN, and we successfully achieved recruitment targets, with a high level of retention in the study. We received good feedback from the practices hosting the study, from patients and from staff; it was an enjoyable and happy study to be involved in for all concerned.

Key outcomes

The study was powered to show the superiority of both active arms over usual care in terms of asthma-related QoL and to show equivalence between the active arms, with equivalence margins being those used in a previous HTA asthma study, which resulted in a *New England Journal of Medicine* publication.[63] Health-related QoL is the outcome measure that best captures the overall effect of asthma on a patient and we used a very well-validated and widely used instrument to measure this key patient-centred factor in our study as the primary outcome. We were indeed able to show superiority of both active treatment arms over usual care and to show equivalence between the two active treatment arms. The improvements in AQLQ scores were observed by the first (3-month) post-intervention assessment and were maintained or increased over the course of the study. We were also able to show lower asthma-related health-care costs in both active treatment arms than in the usual-care arm, which represents a 'dominant' health economic assessment, that is, better outcomes were achieved for lower costs to the NHS. The costs were lowest in the DVD arm, with an 82% chance that usual care was dominated by the provision of the DVD programme.

There was no significant observed change in lung function or in airway inflammation either within or between randomisation treatment arms over the 12 months of the study. There were consistent trends towards modest improvements in asthma symptom scores and other patient-reported outcome measures, asthma attacks, respiratory-related GP consultations and rescue bronchodilator use in the breathing retraining arms compared with the usual-care arm, but none of these reached statistical significance thresholds, other than a low-magnitude improvement in the (already low) depression scores in the DVD treatment arm compared with the usual-care arm. The consistent trends towards improvement with breathing retraining but lack of statistical significance observed for most patient-reported and health resource use measures may indicate that these are chance findings or, more likely, a lack of power of the study to show differences between groups for these outcomes. The reduction in number of asthma attacks is particularly interesting and has not previously been reported in association with breathing retraining, but this study is much larger than previous studies that have been carried out and so is better able to detect a signal. Asthma attacks are

relatively uncommon in patients with mild-to-moderate asthma and so a larger study would be needed to provide a large enough sample to determine whether breathing exercises can indeed reduce asthma exacerbations. However, asthma attacks (as defined by the prescribing of oral corticosteroids for worsening asthma, as recommended by the ERS/ATS Task Force on asthma outcomes)[33] were numerically reduced in this study by approximately one-third in those undergoing breathing retraining. As there was no significant effect on lung function or airway inflammation, it seems that, if a reduction in exacerbations is confirmed in further studies, the mechanism is likely to reflect consulting behaviour and tolerance of symptoms, rather than pathophysiological changes in objective asthma severity. Presented with a patient with asthma attending for worsening asthma symptoms, GPs have limited therapeutic options, and prescription of a course of oral steroids is the most likely action. Some of these episodes may spontaneously resolve without steroids and it is plausible that breathing exercises allowed better symptom control or tolerance on the part of the patient, and so they deferred presentation to a GP, which could have resulted in the prescription of oral steroids. Adverse events were rare, were similar between treatment arms and were of the order of magnitude expected in a 12-month study of this size. There was no suggestion that breathing retraining delivered by either modality caused problems for patients or had any associated adverse events.

The process evaluations confirmed that breathing retraining was acceptable to participants in the study, most of whom felt it to be relevant and useful. Some of the participants in the DVD arm felt that they would liked to have had access to a professional to clarify certain things and to help them through the programme, although the equivalence in outcomes indicates that this was not something that was needed for the breathing retraining to have an effect in this group of patients. We found a NNT of 40 for one patient to benefit from face-to-face physiotherapy compared with the self-guided programme, indicating that for the great majority the self-guided intervention can provide effective breathing retraining. It remains possible that different groups, for example those with more severe asthma or those with more severely impaired QoL, may benefit more from seeing a physiotherapist. Future studies are needed to identify the minority who would benefit from seeing a professional rather than undertaking a self-guided programme.

Clinical relevance and magnitude of effect

We achieved a statistically significant improvement in both active arms compared with usual care, but, as this was a large study, it is important to consider the clinical relevance of the improvements that we observed as well as the statistical significance. The MCID for a patient to notice a difference in QoL is 0.5 for the AQLQ instrument,[24] with a change of 1.0 equating to a large improvement. In both the DVD arm and the physiotherapy arm we observed a mean improvement of 1.1 from baseline, so on average patients felt considerably better with regard to how their asthma was affecting their life. Approximately two-thirds of all patients in both breathing retraining arms achieved the MCID of 0.5 over the study period, with three-quarters reaching the MCID for improvement in the PP population, which may better reflect those who actually received the breathing retraining. In terms of how large or small these improvements are in relation to improvements seen with pharmacological interventions commonly used as add-on treatments to inhaled corticosteroids for people with asthma, we may compare them with those seen in another HTA programme-funded UK primary care pragmatic asthma study reported by Price *et al.*[63] in the *New England Journal of Medicine*, which compared the effectiveness of add-on long-acting beta-agonists (LABAs) with the effectiveness of leukotriene receptor antagonists (LTRAs) in a directly comparable population to that in our study, UK primary care-treated adult asthma patients found by screening to have suboptimally controlled asthma. This study lacked a control arm but, compared with baseline values, the mean improvements in AQLQ score in the ITT population were 1.0 in the LABA group and 0.8 in the LTRA group, so slightly lower than those that we observed with breathing retraining.

In our study, we did observe an improvement in AQLQ score in the usual-care arm of a lesser but large magnitude, with a mean improvement of 0.8 in the ITT population at 12 months and with 56% reaching the MCID threshold. Improvements in QoL are generally seen in the control and placebo arms in asthma RCTs. This improvement is likely to relate partly to the well-described beneficial effects of trial involvement and partly to a 'regression to the mean' effect consequent to our recruitment criterion of impaired QoL.

However, we did find significant improvements over the usual-care arm in both active intervention arms, with the mean improvements over usual care being 0.28 (95% CI 0.11 to 0.44) in the DVD arm and 0.24 (95% CI 0.04 to 0.44) in the physiotherapy arms. Although these levels are below the 0.5 threshold for the MCID, it should be noted that 0.5 relates to the MCID for the individual patient and not for the mean between-group differences. Indeed, it has recently been reported by Bateman *et al.*[64] in a networked meta-analysis of the magnitude of AQLQ changes associated with pharmacological interventions in asthma that this threshold is never reached in RCTs. This study reports the mean improvement in AQLQ score over the control for patients not fully controlled with inhaled corticosteroids as 0.35 (95% CI 0.27 to 0.43) for the addition of a LABA, 0.20 (95% CI 0.13 to 0.27) for the addition of a LTRA, 0.01 (95% CI –0.20 to 0.22) for the addition of theophylline, 0.30 (95% CI 0,20 to 0.40) for the addition of omalizumab and 0.06 (95% CI –0.18 to 0.30) for the addition of a short-acting beta-2 agonist. The improvements over the control that we observed for breathing retraining are therefore of comparable magnitude to those seen with commonly used pharmacological strategies in RCTs, slightly less than those associated with LABAs and slightly greater than those associated with LTRAs.

As recommended by Guyatt *et al.*[32] in the interpretation of AQLQ data in clinical trials, and using the formula that they recommend, we included a NNT for one patient to benefit above usual-care analysis. This provided NNTs of eight for the DVD group and seven for the physiotherapy group, which we could consider low compared with many commonly used interventions in clinical practice.

These findings suggest that breathing retraining has an important and clinically relevant role for patients who are uncontrolled on standard asthma therapy and may be considered as well as, or instead of, an increase in medication. Further studies incorporating 'responder analyses' are needed to clarify whether there are specific characteristics of individual patients to indicate whether a pharmacological or a non-pharmacological adjuvant treatment (or both) will be most effective. The heterogeneity of asthma is increasingly recognised[6] and the concepts of stratified and 'personalised, precision' medicine are increasingly being applied. With the demonstration in our study of the effectiveness of breathing retraining delivered through a simple and cost-effective self-guided intervention, we feel that this could now become a standard treatment option for people with asthma and that breathing dysfunction could be viewed as a 'treatable trait' when personalising treatment for individual patients.[65]

Mechanism of effect

The mechanism of effect of breathing retraining on improving QoL in this study cannot be definitively ascertained, but it does not appear to reflect changes in the pathophysiology of the condition, as reflected by lung function or airway inflammation. Likewise, improvements in anxiety or depression between treatment arms were either not significant or of low magnitude and so cannot fully explain the patient-experienced benefits. It is interesting that asthma symptom scores showed only a trend towards a modest improvement over the study period in those undergoing breathing retraining, which was of lower magnitude (in terms of the MCID) than the change in QoL. This implies that reduced symptoms did not fully explain why patients felt so much better and unaffected by their asthma and may indicate a greater tolerance, understanding and acceptance of the symptoms; these were still present but were less distressing and were accepted and coped with better. It is plausible that the possession of a simple non-pharmacological strategy for dealing with symptoms when they occur provided patients with more confidence and improved self-management skills. Indeed, the qualitative interviews carried out as part of the process evaluation would tend to support this hypothesis.

The AQLQ instrument has four subdomains that can be analysed separately: symptoms, activity, environment and emotions. Other than the activity and environment subdomains in the physiotherapy arm, all of these domains showed statistically significant improvements in both breathing retraining arms compared with the control arm, with the largest magnitude improvements being in the emotions domain. This implies that breathing retraining has a wide-ranging impact on the way that asthma affects a patient, which includes less impact of symptoms and environmental triggers, the ability to undertake higher levels of activity and, in particular, less emotional impact. The mechanism of effect is therefore likely to be complex and multifaceted,

with effects on the perception of symptoms, behaviours and emotions but not on the underlying pathophysiology of the illness.

Patient perspectives and process evaluation

The process evaluation, with both quantitative (questionnaire-based) and qualitative components, showed that patients engaged well with both of the breathing retraining programmes and felt that both the DVD and the booklet were useful. Some participants in the DVD arm felt that they would have liked to see a health professional as part of the retraining process, although the lack of difference in outcomes between the active treatment arms indicates that this was probably not necessary for the majority of patients. As we recruited patients with milder disease from the broad asthma population, who had not actually presented with problems and asked for professional help, it is possible that there remains a subgroup with more severe problems who would gain greater benefits from seeing a physiotherapist in person. However, in the broad asthma population, a simple self-guided programme (a DVD with our theory-based behaviour change booklet) would seem to be capable of providing an inexpensive and convenient intervention for many people with asthma that does not necessitate a commitment of resources to allow far greater access to respiratory physiotherapists in the community.

Adverse events

There have been no suggestions of treatment-related adverse effects from breathing retraining exercises in the literature to date, but in this large study we carried out a careful analysis of any potential downsides for patients undergoing breathing retraining programmes. We collected information on all respiratory adverse events and adverse events that could plausibly be related to the breathing programmes, including musculoskeletal and psychological/psychiatric adverse events, and on all significant adverse events. Overall, the adverse event profile was as expected in the recruited population and adverse events were not felt by the PIs to be study related, with fewer adverse events in the active arms than in the control arm and DVD and physiotherapy programmes appearing to be well tolerated.

Health resource use and asthma-related costs

The asthma-related costs in the study were lower in the active arms than in the usual-care arm, implying that the interventions have the potential to both improve outcomes and reduce costs, with lowest costs in the DVD arm. The main cost items for each group were asthma-related medications and GP consultations. There was no single factor driving the lower costs in the active arms, but we saw trends towards lower GP consultation rates, lower rescue bronchodilator use and lower exacerbation risk. None of these reductions was individually statistically significant when comparing the active arms with the control arm, although the sample size was inadequate to provide sufficient statistical power to test these outcomes. The mean number of respiratory-related GP consultations was 1.8 in the control arm compared with 1.5 in both the physiotherapy arm and the DVD arm and the percentage of participants having one or more asthma attacks requiring oral steroids was 15% in the control arm, 11% in the physiotherapy arm and 9% in the DVD arm. There was an 82% probability of usual care being dominated by the breathing retraining programme delivered by a DVD (lower costs and better outcomes) and the economic evaluation concluded that in this patient sample the self-guided programme was more cost-effective than the provision of face-to-face physiotherapy, by having outcomes within the equivalence margin and costing less.

Strengths and weaknesses of the study

This study has many strengths and a few weaknesses. This is by far the largest study of breathing retraining in asthma to have been reported and we know of no other studies of comparable size currently under way or planned. To our knowledge, this is the first study of breathing retraining in asthma that has compared a face-to-face programme with a self-guided programme and the first to have a rigorous, prospective health economic evaluation and process evaluations embedded within it.

In terms of study design, this study followed two previous smaller studies from the study team[17,19] that together represent an evaluation strategy in keeping with the recommendations of the MRC framework for the evaluation of complex interventions,[38] with this project being a Phase IV study. The study design was a 'pragmatic' RCT, with a focus on confirming the clinical effectiveness and cost-effectiveness of breathing retraining in a broad and representative primary care population. We therefore had wide entry criteria and study procedures that were designed to be as easy to comply with as possible and to interfere with normal care (other than the provision of the interventions) as little as possible. This allowed primary care sites to host the study without too much disruption to usual care and, we believe, encouraged patient participation. We were able to recruit and retain 655 primary care patients into a 12-month study that required informed consent, study visits and questionnaire completion. The study was designed and supervised by a multidisciplinary team, with strong PPI input at all stages provided by our very active PPI representatives and by the patient charity Asthma UK, which was a full partner in the project from its inception. The multidisciplinary team included physiotherapists, primary and secondary care clinicians, scientists, primary and secondary care respiratory nurses, health psychologists, behaviour change experts specialising in developing and evaluating self-guided behaviour change interventions, statisticians and health economists. The involvement of researchers with a general practice background facilitated a study design that was feasible and acceptable in a busy 'routine care' setting and acceptable to patients with mild-to-moderate asthma. The use of an internal pilot allowed hindrances to recruitment and study procedures to be identified and corrected early in the study, with subsequent smooth running of the main trial. Regular steering group meetings were well attended and active, and the team was fortunate to have the support of very interested and active TSC and DMEC members. There was a regular exchange of information with the funder, the National Institute for Health Research (NIHR) HTA programme, as well as the provision of support. Other NIHR structures also provided excellent support to the study. The SCTU undertook trial management most effectively, with several changes in key personnel not impairing the continuity and effectiveness of the team. The friendly, accessible and proactive involvement of the SCTU team was a key strength in delivering a successful study. Invaluable support was provided by the NIHR CRN team involved in the study, with strong support from the research nurse team with regard to the recruitment of practices and patients. There was good partnership with the NHS organisations (clinical commissioning groups and trusts) involved in the study, who also provided support. The general practices hosting the study were invariably supportive and appreciated the pragmatic design of the study and the involvement of practice asthma nurses in the study. Very good feedback was received from the recruiting sites and the GPs, practice nurses and practice managers involved, who were positive about the study and enjoyed their involvement in it. A key strength underlying these effective partnerships was good and open communication throughout the study, allowing 'buy-in' and effective team working. As a result of these good relationships, coupled with a sound study design, we were able to recruit beyond the original recruitment targets and to achieve high retention rates.

Another strength of the study is that we used a variety of clinically relevant outcome measures, including a panel of validated patient-reported outcome measures in questionnaire format, physiological lung function measures (that included quality-assured spirometry measured by trained and accredited respiratory nurses) and airway inflammation measures. In addition, patients provided consent to access their routine primary care medical records, which allowed us to collect consultation, prescribing and other health resource use data. This combination of outcome measures allowed us to assess the effects of the intervention on QoL, the key patient-focused outcome measure that reflects patients' experience of their disease and the amount of disturbance that it causes in their lives, and relate this to other physiological and psychological measures. This multidimensional assessment allows some insight into the mechanisms of effect of this complex intervention and further helps to dispel the myths propagated by some proponents of breathing retraining (such as some of those advocating the Butekyo method) that breathing exercises can 'cure' asthma and replace the need for anti-inflammatory and bronchodilator medication.[66–68] In keeping with our previous studies, we found no significant effect of the interventions on parameters measuring the pathophysiology of asthma, such as lung function and airway inflammation, despite a significant lessening of the impact of asthma on people's lives.

A key strength of the study was the rigorous development process used for transferring the physiotherapy-based programme to a self-guided intervention, with printed support material. The development process that we have described is based on a well-established methodology using an iterative process and extensive and effective patient input. Members of the intervention development team were very experienced, having previously developed a number of effective self-guided interventions in other clinical areas, and applied a tried and tested procedure to develop and refine the materials. The involvement of experienced qualitative researchers allowed patient perspectives to be efficiently and accurately gathered and assessed and to be effectively incorporated into the intervention. A professional media production firm was used to produce the high-quality and patient-friendly self-guided intervention. The self-guided intervention proved to be accessible and well received by patients of all educational levels. The same team designed and performed the process evaluation (including both the qualitative evaluation and the quantitative evaluation), which has contributed to the assessment of the intervention and will inform subsequent implementation work. We were also fortunate to identify experienced local physiotherapists with expertise in breathing retraining who were able to assist with the DVD development and provide the face-to-face physiotherapy intervention.

Similarly, a strength of the study was the involvement of health economists at all stages, from protocol design to writing of the report. The health economic evaluation was seamlessly integrated into the study design and execution. High-quality health economic information is imperative in the current medicopolitical environment if a new intervention is going to be accepted and utilised in clinical care and promoted by commissioners. We believe that the powerful and persuasive health economic arguments, combined with the simplicity and ease of provision of the self-guided intervention, will allow rapid uptake and implementation throughout the NHS, to the benefit of patients.

A further strength of the study was the full involvement of the statistical team at all stages of the project, with input from statisticians on the TSC and the DMEC throughout the study. The choice of primary outcome, primary and secondary statistical analyses and regression models was made with the help of consensus processes after long and constructive debate. The use of the full ITT population in the primary effectiveness analysis, with a number of prespecified sensitivity analyses on the PP population, using different ways of handling missing data and using different regression models, allows confidence to be had in the key messages of the study. The statistically significant superiority of usual care and the equivalence of the self-guided and physiotherapy-based programmes (using prespecified equivalence margins) were maintained in all sensitivity analyses, adding to the confidence that this was a correct finding.

In terms of the limitations of the study, the CONSORT diagram shows that only 10% of the total primary care asthma population invited by post to participate in the study responded to the invitation. It is possible that these respondents represent an atypical sample of patients and that the response to the intervention could be different in the total population. The demographic and asthma severity profile of respondents were, however, typical of those of UK asthma populations. We also feel that our recruitment rate was much higher than that achieved by most asthma studies and it is well documented that the evidence base for asthma guidelines comes from studies with tight inclusion and exclusion criteria that result in $< 2\%$ of all community-treated patients being eligible.[69] One cannot force patients to enter trials and we feel that changes in the design of the study and the processes used would not improve on the recruitment rate that we achieved. However, there is now the need for evaluated implementation studies to confirm that the benefits seen in our 'real-world' but trial-consenting population can be translated to the wider adult asthma population, as the intervention is made available. Such assessments will need to use routinely collected data or minimally intrusive outcome measures if they are to capture outcomes in the wider population.

Approximately 40% of our responders had unimpaired asthma-related QoL and so were ineligible for the study. This is in keeping with previous population-based studies on QoL in asthma, with the majority being found to have impaired health. We feel that those with unimpaired QoL are probably already coping well with their illness and so are not in need of further help from an intervention such as breathing retraining; however, this applies only to a minority of adult asthma sufferers in the UK and so there is potentially a wide use for this intervention in routine practice.

Our study sample size was powered on the primary outcome measure, the AQLQ. For a number of the secondary outcome measures, including asthma attacks, GP consultations and rescue medication prescriptions, we observed numerical, but non-significant or marginally significant, improvements in outcome in the breathing retraining arms compared with the usual-care arm. We cannot say whether these improvements were chance findings or whether lack of statistical power prevented a significant result being seen. This is particularly true of asthma attacks as these occur only in about 1 in 10 patients with mild-to-moderate asthma treated in the community over a single year. Larger studies would be needed to investigate this fully. As all of these factors (consultations, asthma attacks and rescue medication prescriptions) can be assessed through the analysis of routinely collected data, this could be investigated in implementation studies using analysis of anonymised routine data.

Participants in our study were aware of which study arm they had been allocated to. Although this is a limitation, it is clearly not possible to 'blind' a participant in such a study to group allocation. The study was, however, 'observer blinded', with the research nurses collecting data and the statistical team blinded as to study arm allocation until the statistical report was finalised. The control arm in this study consisted of usual care and so those in the active arms had a greater provision of care. Although it is possible that participants randomised to the usual-care arm were disappointed not to be receiving an active intervention, they were assured that at the completion of the study they would be offered the intervention if it was found to be effective. It is noteworthy that there was a large improvement in QoL in the control arm during the study, probably reflecting the beneficial effects of trial involvement and a 'regression to the mean' effect. Those in the DVD arm received audio-visual and printed support materials but there was no provision of additional care, whereas those in the physiotherapy arm underwent three face-to-face visits with a respiratory physiotherapist and also received the printed support materials. Additional professional care can improve health outcomes in a non-specific placebo-like way. In previous studies earlier in the MRC complex intervention framework process, we included additional professional contact in the control arm[17,19] and observed similar improvements in the breathing retraining arm compared with the control arm. As this was a Phase IV pragmatic study, we felt that usual care was the appropriate comparator as it provided a better estimate for the health economic evaluation and provides better information for pragmatic implementation. In this situation the new intervention is provided in addition to current usual care. In our study we did see large improvements in the usual-care arm, although less than in the active arms, reflecting the well-described phenomenon whereby patients benefit simply from taking part in research trials.

Our study included only adults. The intervention materials were designed for adults and would not be transferable to younger age groups without modification. There is anecdotal and very limited study evidence that breathing retraining is feasible and effective in adolescents and in younger children.[70] Asthma has a high prevalence in younger people and there is considerable public and parental interest in non-drug interventions for asthma in children. There is therefore still a need for studies to clarify the clinical effectiveness and cost-effectiveness of breathing retraining interventions in younger people. As we excluded children and adolescents, the groups in whom asthma is most prevalent, the average age of our trial population was higher than that in population-based asthma demographic data. It is possible that there was some under-representation of younger adults, who are generally harder to recruit to time-consuming clinical trials, but the demography in our trial was similar to that in other pragmatic community-based adult asthma clinical trials. For example, in the study by Price *et al.*,[63] the mean age of subjects was 46 years, 56% were aged $\geq$ 46 years and the overall demographic profile was similar to ours.

We were able to provide the intervention only to English-language speakers in this study. There is therefore a need to transfer the intervention into other languages and to frame it in culturally appropriate forms for ethnic minorities. Consideration of adaptations for people with limited literacy skills or learning disabilities is also needed.

Our study provided part of the self-guided intervention in the form of a DVD, although potentially this could be provided in other formats, including for the internet and smartphone-based platforms. The DVD format was chosen, first, to control access to the programme in the trial and, second, as this format was very

commonly used at the time of the study. We had the ability to provide inexpensive DVD players to anyone randomised to this arm of the study who did not already have access to a DVD player, but no one needed this. However, with advances in digital technology and the widespread use of streaming and downloads over the internet, and the wide ownership and use of smartphones, DVDs are now used less frequently. We cannot guarantee that the intervention would provide identical outcomes if provided as an internet-based platform and so this needs to be investigated in further studies. We are currently transferring the content of the DVD to an internet-streamed breathing retraining programme and piloting its use.

Comparison with the results of other studies

The literature on breathing retraining for asthma provided through health professional-delivered face-to-face programmes is reasonably extensive and convincing, such that the UK BTS/SIGN asthma guideline[71] and the WHO GINA guideline[72] both recommend breathing retraining as an option for patients uncontrolled on standard therapy, on the basis of a meta-analysis of the improvement in asthma in RCTs. Our finding that physiotherapy was superior to usual care was therefore in keeping with this evidence base. Our study extends this evidence as the pragmatic design allows greater external validity and confidence in generalising the findings than those of previous studies, which have often used selected populations and atypical clinical settings as opposed to UK general practice. The lack of improvement in lung function and airway inflammation is in accordance with the majority of the current literature, although there are some small studies (some with methodical problems) that have reported improvements in pathophysiological parameters.

Very few previous studies have investigated audio-visual programmes for breathing retraining that do not involve contact with a health professional and none have compared face-to-face breathing retraining with such programmes. The equivalence that we have demonstrated between face-to-face physiotherapy and the DVD programme is therefore a novel finding and of considerable significance in terms of implementing the intervention. Despite the evidence of effectiveness for breathing retraining and the guideline recommendations, the vast majority of patients who could benefit do not currently have access to such training and many who do have to pay a private practitioner (often unregulated) for it.

Other novel aspects of our study include its size, duration and range of outcome measures and the rigorous health economic evaluation and process evaluations. These evaluations suggest that the widespread provision of the self-guided breathing retraining programme is likely to be well accepted and to reduce NHS costs for asthma patients.

Implications for services and future research

We report a Phase IV study of breathing retraining for adults with asthma who are uncontrolled on their current treatment, which has shown improved outcomes and reduced costs of a breathing retraining programme delivered by DVD. On the basis of this evidence, we feel that this intervention is potentially of benefit to the majority of adults with asthma in the community and can be delivered to them as a low-cost, and logistically viable, self-guided programme that has the potential to reduce NHS costs as well as benefit patients. We therefore feel that implementation studies are now needed, to optimise delivery and to assess the effects of providing the intervention in a wide and community-based programme. This has implications for service delivery.

Specific research issues that should be addressed include assessing the effectiveness of the programme delivered though internet-based and smartphone-based platforms. We are currently in the process of carrying out the technical work necessary for this. Comparisons of the acceptability and effectiveness of different delivery methods are needed. We would hope to make these comparisons and are in discussion with our charity partner, Asthma UK, on how to structure and deliver the intervention most effectively.

Given the effectiveness of the intervention in an adult population, we feel that there is a need for research to be carried out in a paediatric population, among whom there is great interest in such interventions. It is not justifiable to automatically extrapolate the results of asthma trials in older age groups to children, although this has frequently been carried out, often inappropriately. In addition, the framing of the intervention and the language and directions provided will need to be adapted for younger people. As mentioned earlier, there is also a need to frame and translate the intervention for specific groups, such as ethnic minorities, those with health literacy problems and those with learning disabilities.

Chapter 8 Conclusions

The majority of adults with asthma have impaired QoL, despite the wide availability of effective pharmacotherapy. Breathing retraining exercises have a good evidence base as adjuvant treatment to improve QoL for people with asthma when taught by a physiotherapist in a face-to-face programme. However, although recommended in national and international guidelines, such programmes are under-used because suitably trained specialist therapists are not available to most people who could benefit. We created a self-guided intervention (DVD plus supporting booklet), involving a multidisciplinary professional team, with extensive patient input, and using a qualitative, iterative methodology. Our aim was to transfer the content of a physiotherapy breathing retraining programme to an attractive and accessible format suitable for patients to use at home, at a time convenient to them. We performed a 12-month, three-armed, parallel-group, observer-blinded RCT involving consenting adults with asthma treated in the community in a primary care setting to compare the effects of the new self-guided intervention with the effects of a three-session face-to-face physiotherapy breathing retraining programme plus the booklet and usual care. Asthma-related QoL was the primary outcome. The study was powered to show the superiority of both breathing retraining programmes over usual care and the equivalence of the self-guided and face-to-face physiotherapy programmes and succeeded in doing so. The improvement in QoL was similar to that reported in a meta-analysis of the effects on QoL of add-on pharmacological interventions for uncontrolled patients. There was no significant change in lung function or airway inflammation associated with breathing retraining by either route, implying that the interventions did not alter the underlying biological pathophysiology of asthma. Consistent (but statistically non-significant) trends in improvement in other patient-reported outcome measures (including symptom scores and anxiety and depression scores) and in asthma attacks, GP consultations and rescue medication use were observed with the active interventions compared with usual care. Both active programmes were well received, acted on and accepted by patients and there was no evidence of adverse effects. Asthma-related health-care costs were lower in both of the active arms than in the usual-care arm, with the self-guided intervention having the lowest costs and a > 80% probability of being the 'dominant' health economic strategy, that is, the strategy with better outcomes at lower costs.

Physiotherapy breathing retraining exercises are therefore acceptable, clinically effective and cost-effective for adults with asthma and may be delivered by a simple self-guided intervention (our DVD plus our theory-based behaviour change booklet). There is now a need for research on effectively implementing this intervention within usual care and to investigate the effects of similar interventions adapted for other patient groups not studied during this project.

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BREATHE trial general practices

- Adelaide Surgery.
- Alma Medical Practice.
- Barton-on-Sea Surgery.
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Contribution of other

Denise Gibson (Consultant Respiratory Physiotherapist) was responsible for the physiotherapy intervention design and development.

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Data sharing statement

Data included in this report can be obtained by contacting the corresponding author.

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Appendix 1 Numbers of patients randomised by study practice and treatment arm

TABLE 54 Numbers of patients randomised by study practice and treatment arm

	Treatment arm, *n*			
Practice	DVD	Physiotherapy	Usual care	Overall, *n*
Adelaide Surgery	1	1	1	3
Alma Medical Practice	3	2	4	9
Barton-on-Sea Surgery	19	9	19	47
Bosmere Medical Practice	14	7	15	36
Brook Lane Surgery	7	4	7	18
Clanfield Surgery	4	2	4	10
Cowplain Family Practice	5	3	5	13
Derby Road Surgery	6	2	5	13
Forest End Surgery	6	3	6	15
Forton Medical Centre	12	6	13	31
Friarsgate Surgery	18	9	19	46
Gosport Medical Centre	8	4	8	20
Heyward Road Surgery	2	1	3	6
Highcliffe Medical Centre	6	3	5	14
Highlands Practice	8	4	7	19
Homewell Practice	13	7	14	34
Kirklands Surgery	7	4	7	18
Lordshill Health Centre	8	4	6	18
New Forest Medical Centre	4	3	4	11
Nightingale Surgery	9	5	9	23
North Baddesley Surgery	4	1	3	8
Old Fire Station Surgery	5	3	6	14
Osborne Practice	9	4	8	21
Park and St Francis Surgery	11	5	10	26
Portsdown Group Practice	18	9	19	46
Ramillies Surgery	4	2	5	11
Regents Park Surgery	3	1	2	6
Ringwood Medical Centre	10	6	10	26
Stoke Road Medical Centre	5	3	6	14
Sunnyside Medical Centre	4	1	4	9

continued

TABLE 54 Numbers of patients randomised by study practice and treatment arm (*continued*)

Practice	Treatment arm, *n*			Overall, *n*
	DVD	Physiotherapy	Usual care	
Three Swans Surgery	7	3	6	16
Waterbrook Medical Practice	9	4	8	21
Waterside Medical Practice	10	6	11	27
Woolston Lodge Surgery	2	1	3	6
Total	261	132	262	655

Appendix 2 Missing baseline primary and secondary outcomes by treatment arm

TABLE 55 Missing baseline primary and secondary outcomes by treatment arm

Outcome	Treatment arm, *n* (%)			Overall (*N* = 655), *n* (%)
	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	
AQLQ	17 (6.5)	12 (9.1)	16 (6.1)	45 (6.9)
Nijmegen questionnaire	2 (0.8)	0 (0.0)	0 (0.0)	2 (0.3)
HADS	4 (1.5)	1 (0.8)	1 (0.4)	6 (0.9)
EQ-5D				
Mobility	2 (0.8)	0 (0.0)	0 (0.0)	2 (0.3)
Self-care	3 (1.1)	1 (0.8)	0 (0.0)	4 (0.6)
Usual activities	2 (0.8)	0 (0.0)	0 (0.0)	2 (0.3)
Pain/discomfort	2 (0.8)	1 (0.8)	1 (0.4)	4 (0.6)
Anxiety/depression	2 (0.8)	0 (0.0)	0 (0.0)	2 (0.3)
EQ-5D VAS	5 (1.9)	1 (0.8)	4 (1.5)	10 (1.5)
ACQ	3 (1.1)	0 (0.0)	0 (0.0)	3 (0.5)
FEV_1	15 (5.7)	2 (1.5)	9 (3.4)	26 (4.0)
FeNO	23 (8.8)	6 (4.5)	20 (7.6)	49 (7.5)
FVC	15 (5.7)	2 (1.5)	9 (3.4)	26 (4.0)
FEV_1-to-FVC ratio	15 (5.7)	2 (1.5)	9 (3.4)	26 (4.0)
FEV_1% predicted	15 (5.7)	2 (1.5)	9 (3.4)	26 (4.0)
PEFR	17 (6.5)	3 (2.3)	13 (5.0)	33 (5.0)
Smoking status	2 (0.8)	0 (0.0)	0 (0.0)	2 (0.3)
Weight	3 (1.1)	0 (0.0)	1 (0.4)	4 (0.6)
Height	2 (0.8)	0 (0.0)	1 (0.4)	3 (0.5)

Appendix 3 Patient withdrawals by treatment arm

TABLE 56 Patient withdrawals by treatment arm

Reason for withdrawal	Treatment arm, *n* (%)			
	DVD (*N* = 261)	Physiotherapy (*N* = 132)	Usual care (*N* = 262)	Total (*N* = 655) *n* (%)
Withdrew from the study	13 (5.0)	3 (2.3)	5 (1.9)	21 (3.2)
Primary reason for withdrawal				
Away for several months	0 (0.0)	1 (33.3)	0 (0.0)	1 (4.8)
No longer wants to take part	1 (7.7)	0 (0.0)	2 (40.0)	3 (14.3)
Did not attend 12-month follow-up	1 (7.7)	0 (0.0)	0 (0.0)	1 (4.8)
Family reasons	1 (7.7)	1 (33.3)	1 (20.0)	3 (14.3)
Husband unwell/family illness	2 (15.4)	0 (0.0)	0 (0.0)	2 (9.5)
Left practice	2 (15.4)	0 (0.0)	0 (0.0)	2 (9.5)
Did not receive DVD	1 (7.7)	0 (0.0)	0 (0.0)	1 (4.8)
Requested to be deleted	1 (7.7)	0 (0.0)	0 (0.0)	1 (4.8)
Notified nurse that since starting the trial asthma worsened	1 (7.7)	0 (0.0)	0 (0.0)	1 (4.8)
Study has not helped asthma	0 (0.0)	1 (33.3)	0 (0.0)	1 (4.8)
Too busy – life commitments	1 (7.7)	0 (0.0)	0 (0.0)	1 (4.8)
Death	1 (7.7)	0 (0.0)	2 (40.0)	3 (14.3)
No reason given	1 (7.7)	0 (0.0)	0 (0.0)	1 (4.8)

Appendix 4 Baseline characteristics of the patient withdrawals and non-withdrawals

TABLE 57 Baseline characteristics of the withdrawals and the non-withdrawals

Characteristic	Withdrawals ($N = 21$)	Non-withdrawals ($N = 634$)
Sex, *n* (%)		
Male	5 (23.8)	231 (36.4)
Female	16 (76.2)	403 (63.6)
Age (years)		
Number included	21	634
Median (IQR)	59 (51.5–64.5)	56 (46–64)
Minimum, maximum	23, 70	16, 70
Weight (kg)		
Number included	21	630
Median (IQR)	77 (68–90)	81.42 (18–46)
Minimum, maximum	54, 118	
Height (cm)		
Number included	21	630
Median (IQR)	161.5 (157–170)	166.56 (9.06[a])
Minimum, maximum	152, 175	
Smoking status, *n* (%)		
Current smoker	0 (0.0)	50 (7.9)
Previous smoker	6 (28.6)	212 (33.4)
Never smoker	15 (71.4)	370 (58.4)
What they currently smoke, *n* (%)		
Cigarettes	0 (0.0)	33 (5.2)
Tobacco	0 (0.0)	18 (2.8)
Cigars	0 (0.0)	1 (0.2)
What they used to smoke, *n* (%)		
Cigarettes	5 (23.8)	191 (30.1)
Tobacco	0 (0.0)	10 (1.6)
Cigars	1 (4.8)	1 (0.2)
Cigarettes/tobacco	0 (0.0)	4 (0.6)
Cigarettes/cigars	0 (0.0)	4 (0.6)
Tobacco/cigars	0 (0.0)	1 (0.2)
Cigarettes/tobacco/cigars	0 (0.0)	1 (0.2)

continued

TABLE 57 Baseline characteristics of the withdrawals and the non-withdrawals (*continued*)

Characteristic	Withdrawals (*N* = 21)	Non-withdrawals (*N* = 634)
Average cigarettes/day for ever smokers, *n*		
Median (IQR)	10 (6.5–20)	15 (8–20)
Minimum, maximum	5, 20	1, 100
Pack-years of smoking		
Number included	6	238
Median (IQR)	23.25 (6.5–57.25)	11.85 (3–25)
Minimum, maximum	2, 100	0.05, 300
Age diagnosed with asthma (years)		
Number included	21	629
Median (IQR)	37 (14–52)	28 (11–45)
Minimum, maximum	3, 60	1, 68
Family history of asthma, *n* (%)		
Mother		
Yes	3 (14.3)	103 (16.2)
No	18 (85.7)	513 (80.9)
Unknown	0 (0.0)	13 (2.1)
Father		
Yes	2 (9.5)	72 (11.4)
No	17 (81.0)	528 (83.3)
Unknown	2 (9.5)	29 (4.6)
Siblings		
Yes	6 (28.6)	157 (24.8)
No	14 (66.7)	426 (67.2)
n/a	0 (0.0)	43 (6.8)
Children		
Yes	4 (19.0)	202 (31.9)
No	15 (71.4)	305 (48.1)
n/a	2 (9.5)	123 (19.4)
Other family members		
Yes	5 (23.8)	226 (35.6)
No	15 (71.4)	379 (59.8)
Unknown	1 (4.8)	11 (1.7)
Asthma triggers, *n* (%)		
Cats	13 (61.9)	275 (43.4)
Dogs	8 (38.1)	170 (26.8)
Dust	16 (76.2)	521 (82.2)
Exercise	14 (66.7)	462 (72.9)
Pollen	13 (61.9)	417 (65.8)

TABLE 57 Baseline characteristics of the withdrawals and the non-withdrawals (*continued*)

Characteristic	Withdrawals (*N* = 21)	Non-withdrawals (*N* = 634)
Smoke	13 (61.9)	444 (70.0)
Stress	10 (47.6)	323 (50.9)
Food	5 (23.8)	128 (20.2)
Others	17 (81.0)	484 (76.3)
FeNO (p.p.b.)		
Number included	18	588
Median (IQR)	21.5 (15.75–32.75)	22 (14–34)
Minimum, maximum	5, 202	0, 159
FEV_1 (l)		
Number included	20	609
Median (IQR)	2.3 (1.9–2.9)	2.6 (0.8[a])
Minimum, maximum	1.5, 4.1	
FVC (l)		
Number included	20	609
Median (IQR)	3.0 (2.3–3.5)	3.4 (0.9[a])
Minimum, maximum	2.1, 5.0	
FEV_1-to-FVC ratio		
Number included	20	609
Median (IQR)	0.8 (0.8–0.9)	0.8 (0.1[a])
Minimum, maximum	0.6, 0.9	
FEV_1% predicted		
Number included	20	609
Median (IQR)	90.5 (77.8–103.8)	90.7 (20.0[a])
Minimum, maximum	69, 112	
PEFR		
Number included	20	602
Median (IQR)	406.0 (355–529)	422.2 (117.1[a])
Minimum, maximum	292, 623	

n/a, not applicable; p.p.b., parts per billion.
a SD.

Appendix 5 Supplementary information and sensitivity analyses on rescue inhaler use

TABLE 58 Distribution of rescue inhaler use by treatment arm in the 12 months post randomisation in the PP population

	Treatment arm, *n*			
Number of rescue inhalers	DVD	Physiotherapy	Usual care	Total, *n*
0	63	22	44	129
1	30	22	57	109
2	31	13	28	72
3	18	16	23	57
4	21	12	23	56
5	16	3	10	29
6	10	6	9	25
7	5	2	5	12
8	6	3	11	20
9	4	2	3	9
10	5	1	5	11
11	1	0	1	2
12	1	3	5	9
13	1	2	0	3
14	1	2	0	3
16	1	0	1	2
17	0	0	1	1
18	0	0	2	2
22	0	0	2	2
26	0	0	1	1
28	1	0	0	1
40	0	1	0	1
Total	215	110	231	556

TABLE 59 Unadjusted analysis of the negative binomial regression for rescue inhaler use in the 12 months post randomisation in the PP population

Comparison	Unadjusted IRR	95% CI	*p*-value
Physiotherapy vs. usual care	1.04	0.80 to 1.35	0.76
DVD vs. usual care	0.86	0.69 to 1.07	0.18
DVD vs. physiotherapy	0.83	0.63 to 1.08	0.17

TABLE 60 Adjusted analysis of the negative binomial regression for rescue inhaler use in the 12 months post randomisation in the PP population

Comparison	Adjusted IRR[a]	95% CI	*p*-value
Physiotherapy vs. usual care	1.04	0.78 to 1.40	0.94
DVD vs. usual care	0.93	0.73 to 1.19	0.78
DVD vs. physiotherapy	0.89	0.66 to 1.21	0.66

a Adjusted for age, sex, BTS treatment step, baseline smoking status, baseline HADS scores and baseline Nijmegen score.

Appendix 6 Supplementary information and sensitivity analyses on asthma exacerbation frequency

TABLE 61 Group differences in asthma exacerbations in the 12 months post randomisation in the PP population[a]

	Treatment arm, *n*			
Oral corticosteroid courses	DVD	Physiotherapy	Usual care	Total, *n*
0	193	97	195	485
1	16	9	26	51
2	2	3	8	13
3	2	0	1	3
4	2	1	0	3
10	0	0	1	1
Total	215	110	231	556

a Adjusted for exacerbations in the previous 12 months, age, sex, BTS treatment step and smoking status.

TABLE 62 Unadjusted analysis of the negative binomial regression for asthma exacerbations in the 12 months post randomisation in the PP population

Comparison	Unadjusted IRR	95% CI	*p*-value
Physiotherapy vs. usual care	0.73	0.35 to 1.50	0.38
DVD vs. usual care	0.66	0.37 to 1.20	0.18
DVD vs. physiotherapy	0.92	0.43 to 1.95	0.82

TABLE 63 Adjusted analysis of the negative binomial regression for asthma exacerbations in the 12 months post randomisation in the PP population

Comparison	Adjusted IRR[a]	95% CI	*p*-value
Physiotherapy vs. usual care	0.79	0.33 to 1.90	0.81
DVD vs. usual care	0.69	0.33 to 1.42	0.45
DVD vs. physiotherapy	0.87	0.34 to 2.19	0.93

a Adjusted for age, sex, BTS treatment step and smoking status.

Appendix 7 Numbers of participants in the per-protocol population having none or one or more respiratory-related general practitioner consultations in the 12 months post randomisation

TABLE 64 Numbers of participants in the PP population having none or one or more respiratory-related GP consultations in the 12 months post randomisation by treatment group

	Treatment arm, *n*			
Number of GP consultations	DVD	Physiotherapy	Usual care	Total, *n*
None	52	25	45	122
≥ 1	163	85	186	434
Total	215	110	231	556

Appendix 8 Supplementary information and sensitivity analyses on the primary outcome (Asthma Quality of Life Questionnaire)

TABLE 65 12-month adjusted change in AQLQ score in the DVD, physiotherapy and usual-care treatment arms in the ITT population

	Treatment arm, adjusted mean difference[a] (95% CI)			Adjusted mean difference[b] (95% CI)
AQLQ subdomain	Physiotherapy[c] vs. usual care	DVD vs. usual care	DVD vs. physiotherapy[c]	DVD vs. physiotherapy[c]
Total	0.22 (0.003 to 0.43)*	0.28 (0.12 to 0.45)*	0.07 (–0.15 to 0.28)	0.03 (–0.20 to 0.27)
Symptoms	0.25 (0.01 to 0.49)*	0.24 (0.05 to 0.43)*	–0.01 (–0.25 to 0.24)	–0.01 (–0.28 to 0.25)
Activities	0.07 (–0.17 to 0.30)	0.23 (0.05 to 0.41)*	0.16 (–0.07 to 0.40)	0.13 (–0.13 to 0.38)
Emotion	0.37 (0.08 to 0.65)*	0.38 (0.16 to 0.60)**	0.01 (–0.28 to 0.30)	0.02 (–0.29 to 0.33)
Environment	0.21 (–0.06 to 0.48)	0.33 (0.11 to 0.54)*	0.12 (–0.16 to 0.39)	0.09 (–0.20 to 0.39)

*$p \leq 0.05$, **$p < 0.001$.
a Adjusted for prespecified list of covariates.
b Adjusted for prespecified list of covariates along with a new covariate – amount of practice.
c Excluding participants who did not engage with the breathing retraining at 3 months.

TABLE 66 3-month adjusted change in AQLQ score in the DVD, physiotherapy and usual-care treatment arms on the ITT population

	Treatment arm, adjusted mean difference[a] (95% CI)			Adjusted mean difference[b] (95% CI)
AQLQ subdomain	Physiotherapy[c] vs. usual care	DVD vs. usual care	DVD vs. physiotherapy[c]	DVD vs. physiotherapy[c]
Total	0.41 (0.20 to 0.63)**	0.29 (0.11 to 0.47)**	–0.12 (–0.35 to 0.10)	–0.10 (–0.34 to 0.13)
Symptoms	0.51 (0.26 to 0.76)**	0.38 (0.18 to 0.59)**	–0.13 (–0.38 to 0.13)	–0.09 (–0.36 to 0.17)
Activities	0.24 (–0.001 to 0.48)*	0.29 (0.09 to 0.48)*	0.05 (–0.20 to 0.30)	0.03 (–0.22 to 0.29)
Emotion	0.42 (0.13 to 0.71)*	0.23 (–0.01 to 0.47)	–0.19 (–0.49 to 0.11)	–0.13 (–0.44 to 0.18)
Environment	0.42 (0.15 to 0.70)**	0.26 (0.03 to 0.49)*	–0.17 (–0.45 to 0.12)	–0.16 (–0.46 to 0.13)

*$p \leq 0.05$, **$p < 0.001$.
a Adjusted for prespecified list of covariates.
b Adjusted for prespecified list of covariates along with a new covariate – amount of practice.
c Excluding participants who did not engage with the breathing retraining at 3 months.

Appendix 9 Adverse event categories

- Abdominal/gastrointestinal: vaginal discharge, testicular pain, rectal bleeding, abdominal pain – complains of adhesions, altered bowel habit – complains of adhesions, diarrhoea, menorrhagia, bacterial vaginosis, amenorrhoea, gastric band erosion, laparoscopic vaginal hysterectomy, gastritis, vaginal discharge, oral thrush, haemorrhoids, vaginal thrush, suspected urinary tract infection, vulvovaginal candidiasis, epigastric pain plus dysfunctional breathing, pain from pre-existing umbilical hernia, caecal volvulus, small bowel obstruction, colitis, vomiting, vomiting (flu), non-specific abdominal pain, gastric bypass surgery, irritable bowel syndrome, abdominal cramps and diarrhoea, epigastric pain episode linked to ongoing acid reflux, abdominal cramps – gastroenteritis, lower abdominal pain, abdominal pain, breathlessness related to abdominal pain, increased nausea, abdominal pain (right iliac fossa), lower abdominal pain with loose stools, per vaginal bleed post large loop excision of the transformation zone of the cervix, small bowel obstruction, ileus, umbilical hernia repair.
- Acute exacerbation of asthma: acute asthma exacerbation, asthma exacerbation, exacerbation of asthma/COPD, asthma flair, green sputum worsening (acute exacerbation of asthma), productive cough worsening (acute exacerbation of asthma), mild exacerbation of asthma, chesty cough (acute asthma exacerbation), cough/wheeze (infected exacerbation of asthma), asthma attack, chest infection/asthma exacerbation, infective exacerbation of asthma.
- Chest pain and cardiovascular: chest pain, chest pains, chest pains with palpitations, chest wall pain, costochondritis, chest pain? – hiatus hernia, rib pain, chest pain – acute coronary syndrome, myocardial infarction, chest pain secondary to indigestion, exertional chest pain (while hovering), chest pain (musculoskeletal), dull pain around right lateral chest wall, pleuritic left-sided chest pain.
- Increased asthma symptoms: cough, wheeze tachycardia, worsening of asthma, wheeze, chest tightness, wheeze plus shortness of breath, shortness of breath, mild wheeze, shortness of breath on exertion, cough, dyspnoea, asthma triggered by pollen, ongoing asthma symptoms, wheezy cough, acute wheezy bronchitis, respiratory symptoms limiting exercise activities, poor asthma control, nocturnal cough/wheeze, feels unable to fully inhale.
- Malignancy: malignant lymphoma, malignant neoplasm breast – review, prostate cancer, follicular papillary carcinoma.
- Musculoskeletal: Baker's cyst, cervicalgia, golfer's elbow, degenerative change in lumbosacral region, left leg pain, lacerated left middle finger, back pain, aching muscles, shoulder pain, left arm pain, leg cramps, back pain following fall, arthralgia of hands/shoulders, knee pain, shoulder pain, tennis elbow, lateral epicondylitis, ankle pain, ankle and hip pain, sprain (left) lateral collateral knee ligament, hip pain, acute lumbar back pain, sprain (left) lateral collateral ligament, neck pain, joint aches (virus), joint ache, right knee replacement surgery, left-sided jaw pain, neck pain, lower back pain, fracture of lower vertebra, right shoulder rotator cuff tear, gout, fractured right rib, prolapsed intervertebral lumbar disc (worsening of), right shoulder rotator cuff sprain, right bicep tendon rupture, frozen shoulder (right), worsening of frozen shoulder (right), rotator cuff syndrome, left-sided muscle tightness in neck, septic arthritis.
- Neurological: tremor, right-hand numbness, headache – different from migraine, neuralgic pain, neuropathic pain, headache, right-sided body numbness, transient ischaemic attack, chronic inflammatory demyelinating polyneuropathy, fatigue, dizziness, double vision, nausea, cerebral venous thrombosis, left-sided numbness, tinnitus, giant cell arteritis, post-FeNO test breathlessness, light-headedness and clammy, migraine.
- Psychological/psychiatric: shortness of breath (panic attack), anxiety, depression, insomnia, low mood, panic attacks, recurrence of depressive episode, low mood, overbreathing, stress.
- Respiratory tract infection/cough: acute laryngitis, bibasilar collapse, bronchitis, chest infection, chest infection/shortness of breath on exertion, chest rattle, chesty cough, cold, cold virus – hoarseness and cough, cold virus – sore throat and cough, congestion with cold, cough and shortness of breath, coryzal, cough (flu), cough (post viral), cough (upper respiratory tract infection), cough? – viral laryngitis, cough with green phlegm, wheeze, shortness of breath, crackles and phlegm, cough/cold,

dry cough, ear infection, fever (flu), flu-like virus, green sputum, green sputum (upper respiratory tract infection), haemoptysis, influenza A, laryngitis, lower respiratory tract infection, mild cough, night cough, pharyngitis, pleural effusion, pneumonia, post viral cough and wheeze, productive cough, productive cough (lower respiratory tract infection), *Pseudomonas* – chest infection, *Pseudomonas aeruginosa* infection, respiratory heart infection, respiratory tract infection, shortness of breath (pneumonia), sore throat (virus), stridor, upper respiratory chest infection, viral cold and cough, viral illness causing wheeze, fever, chest tightness, viral infection, viral upper respiratory tract infection, worsening cough with wheeze and shortness of breath.

- Rhinitis/rhinosinusitis: (sinusitis) blocked nose, (sinusitis) earache, (sinusitis) sore eyes, acute sinusitis, allergic rhinitis, blocked ear – left sided, catarrh, chronic rhinitis, congestion, earache/congested sinuses, Eustachian tube dysfunction, inflamed left ear canal, nasal congestion, otitis media, post-nasal drip, runny nose, sinusitis, worsening hay fever, worsening of otitis externa.
- Miscellaneous: acute tonsillitis, anaemia, balanitis, benign paroxysmal positional vertigo, blepharitis, calf pain, chalazion (eyelid cyst), conjunctivitis, contact dermatitis, contraception, cough? gastric reflux? post-nasal drip, dysfunctional breathing, Eustachian tube dysfunction (bilateral), excision of thyroglossal cyst, eye symptoms, facial pain, fever, flu symptoms, heterozygous factor V Leiden mutation, hoarseness, itch, left otalgia, neck swelling, occasional feeling below sternum of 'racing' – fluttering, feels winded, open wound on scalp, oral thrush, otitis externa, pleural effusion, post-spirometry chest discomfort, problems with crumbling teeth, pyrexia (virus), scolding injury, seborrheic dermatitis, sensation of mucus in throat, snoring symptoms, swollen tongue, tight/sore throat, tonsillitis, urinary tract infection, urticarial rash, virus affecting ears, throat and stomach, watery eyes.

Appendix 10 List of all serious adverse events reported

TABLE 67 List of all serious adverse events (SAEs) reported

Arm	Patient ID	Date of onset of SAE	Main symptom	Serious[a]	Causality[b]
DVD	11011	14 January 2013	Gastric band erosion	3	5
	11023	30 December 2012	Chest pain	3	5
	12114	03 April 2014	Acute exacerbation of asthma	3	3
	15207	26 November 2013	Chest pain (musculoskeletal)	3	5
	17121	08 August 2013	Non-specific abdominal pain	3	5
	20244	07 February 2014	Asthma exacerbation	3	3
	21269	09 March 2014	Transient ischaemic attack	3	3
	31447	03 March 2015	Abdominal pain	3	5
	32446	05 June 2015	Chest infection/coronary artery disease	3	3
	39613	20 July 2015	Acute exacerbation of asthma	3	3
	40596	05 June 2015	Death – cardiac arrest	1	5
Physiotherapy	10014	17 April 2013	Malignant lymphoma	2	5
	12067	28 October 2013	Chest pain with palpitations	3	5
	38576	17 November 2014	Septic arthritis	3	5
	38582	16 March 2015	Asthma exacerbation	3	3
Usual care	12057	24 May 2014	Hospitalised – chest infection	3	3
	12091	28 December 2013	Chest pain	3	5
	12127	31 October 2013	Gastritis	3	5
	12195	26 May 2014	Chest pain secondary to hiatus hernia	3	5
		01 September 2014	Abdominal pain		
	14095	26 April 2014	Death – pulmonary oedema	1	5
	15203	16 June 2014	Caecal volvolus	3	5
		31 July 2014	Colitis		
	17173	23 July 2014	Pneumonia	3	3
	18184	02 March 2014	Stridor	3	5
	20238	11 April 2014	Death – pleural effusion	1	5
	25294	27 July 2014	Urinary tract infection	3	3
	30395	26 December 2014	Influenza A	3	5
	31434	24 March 2015	Pneumonia	3	4
	31501	04 July 2014	Cerebral venous thrombosis	3	3

continued

TABLE 67 List of all serious adverse events (SAEs) reported (*continued*)

Arm	Patient ID	Date of onset of SAE	Main symptom	Serious[a]	Causality[b]
	32449	10 September 2014	Acute coronary syndrome	3	5
	34477	24 December 2014	Chest pain – non cardiac	3	5
		27 June 2014			
		22 June 2014			
	37547	15 July 2015	Per vaginal bleed post large loop excision of the transformation zone of the cervix	3	5
	38570	22 November 2014	Pulmonary embolism	2	5
		02 December 2014	Lower respiratory tract infection		
	38572	14 February 2015	Small bowel obstruction	3	5
	38587	10 September 2015	Tonsillitis	3	5
	39575	09 January 2015	Infective exacerbated asthma	3	3

a Why was the event serious?: 1 = resulted in death, 2 = life-threatening, 3 = required hospitalisation or prolongation of existing hospitalisation, 4 = resulted in persistent or significant disability/incapacity, 5 = congenital anomaly/birth defect.
b Investigator's opinion – causal relationship to SAE: 1 = definitely, 2 = probably, 3 = possibly, 4 = unlikely, 5 = not related.

Appendix 11 List of all adverse events (maximum grade) reported by treatment arm

TABLE 68 List of all adverse events (maximum grade) reported (as categorised by PIs) in the DVD arm

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
Abdominal/ gastrointestinal	Testicular pain	10004	11 October 2013	2		5
	Gastric band erosion	11011	14 January 2013	3	3	5
	Haemorrhoids	13051	06 May 2014	3		5
	Suspected urinary tract infection	13053	11 June 2014	2		5
	Pain from pre-existing umbilical hernia	15201	UNK May 2013	2		5
	Non-specific abdominal pain	17121	08 August 2013	2	3	5
	Irritable bowel syndrome	24307	15 October 2014	1		5
	Abdominal cramps and diarrhoea	25303	18 December 2014	1		4
	Abdominal cramps – gastroenteritis	27466	30 May 2015	2		5
	Abdominal pain	31447	23 March 2015	3	3	5
	Breathlessness related to abdominal pain	32409	17 April 2015	2		5
Acute exacerbation of asthma	Acute exacerbation of asthma	10003	11 February 2013	2		3
	Asthma exacerbation	10031	11 July 2013	2		3
	Exacerbation of COPD	12064	03 March 2014	2		3
	Acute asthma exacerbation	12114	03 April 2014	3		3
	Asthma flair	15157	29 August 2014	1		3
	Asthma exacerbation	19221	UNK February 2014	1		3
	Asthma exacerbation	20244	07 February 2014	2	3	3
	Exacerbation of asthma	31433	09 January 2015	1		3
	Acute exacerbation of asthma	31453	21 April 2015	2		3
	Acute respiratory distress syndrome	32446	05 June 2015	3	3	3
	Cough/wheeze (infected exacerbation of asthma)	33511	15 December 2014	2		3
	Acute exacerbation of asthma	33521	27 December 2014	1		3
	Acute exacerbation of asthma	33522	UNK February 2015	2		3
	Asthma exacerbation	34476	15 May 2015			3

continued

TABLE 68 List of all adverse events (maximum grade) reported (as categorised by PIs) in the DVD arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Acute exacerbation of asthma	34516	22 June 2015	2		3
	Asthma attack	35545	15 August 2015	2		3
	COPD exacerbation	36529	22 March 2015	3		3
	Exacerbation of asthma	37538	15 December 2014	2		3
	Asthma exacerbation	38562	17 March 2015	2		3
	Asthma exacerbation	39613	20 July 2015	3	3	3
Chest pain and cardiovascular	Atrial fibrillation	10020	23 March 2013	2		5
	Chest pain	11023	30 December 2012	2	3	5
	Hypertension	13053	30 October 2013	3		5
	Chest pain (musculoskeletal)	15207	26 November 2013	2	3	5
	Chest pain	17108	25 January 2014	2		4
	chest pain	24307	26 May 2014	2		4
	Palpitations	31481	17 March 2015	1		4
	Chest pain related to abdominal pain	32409	17 April 2015	2		5
	Cardiac disorder	32446	26 May 2015	4	3	5
	Chest soreness	39613	01 November 2015	1	3	3
	Cardiac arrest	40596	05 June 2015	5		5
	Palpitations	40609	26 February 2015	1		5
	Left lateral chest wall pain	40614	02 December 2015	1		5
Increased asthma symptoms	Worsening of asthma	12114	24 February 2014	1		3
	Worsening of asthma	13053	06 August 2013	2		3
	Cough	15157	09 June 2014	1		3
	Wheeze	16136	UNK April 2014	1		3
	Cough	16160	31 March 2014	1		3
	Shortness of breath	18172	18 October 2013	1		3
	Cough	18172	28 May 2014	1		3
	Cough	19221	UNK February 2014	1		3
	Cough	21269	06 March 2014	1		3
	Cough	23300	27 December 2014	1		3
	Cough	25298	01 November 2014	1		3
	Shortness of breath from hay fever	25308	09 June 2014	1		3
	Wheezy cough	25332	01 April 2014	1		3
	Cough	26336	24 June 2014	1		3
	Tight chest	30391	13 October 2014	1		3
	Increasing shortness of breath	31401	15 May 2014	2		3
	Poor asthma control	31455	UNK November 2014	1		3

TABLE 68 List of all adverse events (maximum grade) reported (as categorised by PIs) in the DVD arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Worsening of asthma	32451	UNK February 2015	2		3
	Shortness of breath	34438	15 September 2014	1		3
	Cough	34476	24 December 2014	1		3
	Cough/wheeze	34516	15 May 2015	1		3
	Worsening of asthma (cough and wheeze)	37539	05 December 2014	3		3
	Chest tightness	37549	20 February 2015	2		3
	Feels unable to fully inhale	38562	11 October 2015	2		3
Malignancy	Malignant neoplasm breast – review	13051	01 April 2014	3		5
	Prostate cancer	24289	05 January 2015	3		5
	Follicular papillary carcinoma	30426	21 May 2014	4	3	5
Musculoskeletal	Baker's cyst	10003	30 September 2013	1		5
	Golfer's elbow	10004	11 February 2013	2		4
	Lacerated left middle finger	10020	23 September 2013	1		5
	Aching muscles	10033	06 August 2013	1		5
	Left arm pain	12064	17 September 2013	2		4
	Leg cramps	12085	06 May 2014	1		5
	Back pain following fall	12089	20 June 2014	2		5
	Lateral epicondylitis	13051	06 May 2014	3		5
	Right shoulder rotator cuff strain	31433	14 October 2014	2		5
	Neck pain	33522	UNK November 2014	2		4
	Spinal stenosis	40596	13 March 2015	2		5
	Right frozen shoulder	40598	01 May 2015	1		5
	Back pain	42618	28 October 2015	2		5
	Lower back pain	42629	19 August 2015	1		5
	Hip pain	43651	02 July 2015	1		5
Neurological	Right-hand numbness	12049	31 October 2013	1		4
	Headache – different from migraine	12089	07 November 2013	2		4
	Right-sided body numbness	21269	09 March 2014	4		4
	Transient ischaemic attack	21269	09 March 2014	3	3	5
	Fatigue	31420	27 November 2014	1		4
	Dizziness	33495	22 September 2014	2		4
	Tinnitus	36535	UNK April 2015	2		5

continued

TABLE 68 List of all adverse events (maximum grade) reported (as categorised by PIs) in the DVD arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
Psychological/ psychiatric	Anxiety with depression	13045	30 December 2013	2		3
	Insomnia	13051	04 October 2013	3		3
	Depression	16136	UNK September 2013	2		3
	Depression	20248	01 September 2014	1		3
	Depression	22275	UNK January 2014	1		3
	Anxiety	32404	UNK March 2015	1		3
	Anxiety	35540	28 December 2014	1		3
	Depression	35545	UNK May 2015	2		3
	Low mood	38580	UNK January 2015	1		3
	Memory loss	40596	22 December 2014	2		3
	Anxiety attack	43637	21 October 2015	1		3
Respiratory tract infection/cough	Chest infection	12064	21 May 2014	2		5
	Chesty cough	12114	11 October 2013	2		5
	Upper respiratory tract infection	13061	26 September 2013	1		4
	Chest infection	15155	31 December 2013	1		4
	Chest infection	15157	07 May 2014	1		5
	Productive cough	16136	UNK April 2014	1		5
	Green sputum	16160	03 April 2014	1		5
	Chesty cough	17108	08 April 2014	2		4
	Laryngitis	17144	16 December 2013	1		5
	Worsening of cough	18172	13 June 2014	1		5
	Bronchitis	19221	UNK November 2013	1		5
	Chest infection	20249	12 April 2014	1		5
	Cold	21269	04 November 2014	1		5
	Cold	23315	01 January 2015	1		5
	Upper respiratory tract infection	23316	13 March 2014	1		5
	Chest infection	23359	23 January 2015	1		5
	Chest infection	24289	15 July 2014	1		5
	Viral cough	25332	14 December 2014	1		5
	Lower respiratory tract infection	25376	25 December 2014	1		5
	Viral infection	26323	18 January 2015	1		5
	Chest infection	26374	02 December 2014	1		5
	Upper respiratory tract infection	27337	05 July 2014	1		5
	Cold	27367	05 October 2014	1		5
	Upper respiratory tract infection	27466	05 January 2015	2		5
	Sore throat	29463	08 December 2014	1		5

TABLE 68 List of all adverse events (maximum grade) reported (as categorised by PIs) in the DVD arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Chesty cough	30391	24 March 2015	1		5
	Productive cough	31401	07 November 2014	2		4
	Upper respiratory tract infection	31420	29 December 2014	2		4
	Chest infection	31447	09 June 2015	2		4
	Upper respiratory tract infection	31481	01 February 2015	1		4
	Chest infection	32407	UNK December 2014	2		5
	Chest infection	32446	05 June 2015	3	3	5
	Lower respiratory tract infection	32451	11 March 2015	2		5
	Chesty cough	33511	26 January 2015	2		4
	Productive cough (lower respiratory tract infection)	33520	10 December 2014	1		4
	Chest infection	33521	12 December 2014	1		4
	Cold	33522	UNK February 2015	1		4
	Upper respiratory tract infection	34456	22 May 2015	2		5
	Cough and hoarse voice	34476	16 January 2015	2		5
	Worsening cough with wheeze and shortness of breath	34516	02 October 2014	2		4
	Cold	35531	01 December 2014	1		5
	Upper respiratory tract infection	35540	01 January 2015	2		4
	Sore throat	36554	30 July 2015	1		5
	Post viral cough and wheeze	37549	06 January 2015	2		5
	Viral cold and cough	38560	28 December 2014	1		5
	Chest infection/shortness of breath on exertion	38561	02 January 2015	2		4
	Chest infection	38579	09 April 2015	2		5
	Cold virus – hoarseness and cough	38580	08 October 2015	1		5
	Chest infection	38592	19 May 2015	2		4
	Cough	38602	11 December 2014	2		5
	Cough and brown phlegm	39613	08 December 2014	2		5
	Upper respiratory tract infection	41648	20 December 2015	1		5
	Lower respiratory tract infection	42618	20 April 2015	1		5
	Acute bronchitis	43638	18 November 2015	1		5
	Cough	43646	23 March 2015	1		5

continued

TABLE 68 List of all adverse events (maximum grade) reported (as categorised by PIs) in the DVD arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Chest infection	43651	03 January 2016	1		5
	Cough	43652	05 January 2016	2		5
Rhinitis/rhinosinusitis	Chronic rhinitis	10031	07 August 2013	2		5
	Worsening hay fever	12114	23 May 2014	1		5
	Otitis media	13051	17 January 2014	3		5
	Nasal congestion	15155	17 August 2013	1		4
	(Sinusitis) sore eyes	16196	26 December 2013	1		5
	Inflamed left ear canal	23316	18 February 2014	1		5
	Sinusitis	25308	25 January 2015	1		5
	Congestion	29463	08 December 2014	1		5
	Worsening of otitis externa	31401	15 May 2014	2		5
	Eustachian tube dysfunction	31447	10 December 2014	1		4
	Earache	34476	26 March 2015	1		5
	Acute sinusitis	35531	01 December 2014	2		4
	Blocked ear	36535	UNK April 2015	2		5
	Post-nasal drip	38568	08 May 2015	2		4
	Eustachian tube dysfunction	43638	08 October 2015	1		5
Miscellaneous	Watery eyes	10004	08 April 2013	2		5
	Scolding injury	10020	02 October 2013	1		5
	Eye symptoms	10033	31 October 2013	1		5
	Occasional feeling below sternum of 'racing' – fluttering, feels winded	12085	06 May 2014	1		5
	Urticarial rash	13045	13 January 2014	2		5
	Urinary tract infection	13051	30 May 2014	2		5
	Snoring symptoms	13052	02 January 2014	2		5
	Facial pain	20244	07 March 2014	1		4
	Benign paroxysmal positional vertigo	29463	25 June 2014	1		4
	Sensation of mucus in throat	31435	UNK September 2014	2		4
	Facial pain	34476	26 March 2015	1		5
	Post-spirometry chest discomfort	37549	02 September 2014	1		5
	Temporomandibular joint disorder	38597	UNK February 2015	3		5
	Blocked ear right	38603	UNK April 2015	1		5
	Lower back pain (secondary to car accident in 2006)	38622	10 July 2015	1		5
	Claudication left calf	40596	26 January 2015	1		5

TABLE 68 List of all adverse events (maximum grade) reported (as categorised by PIs) in the DVD arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Fever	42629	30 August 2015	1		5
	Vertigo	43631	21 June 2015	1		5

UNK, unknown.
a Grade: 1 = mild, 2 = moderate, 3 = severe, 4 = life-threatening, 5 = death related to adverse event.
b Why was the event serious?: 1 = resulted in death, 2 = life-threatening, 3 = required hospitalisation or prolongation of existing hospitalisation, 4 = resulted in persistent or significant disability/incapacity, 5 = congenital anomaly/birth defect.
c Investigator's opinion – causal relationship to adverse event: 1 = definitely, 2 = probably, 3 = possibly, 4 = unlikely, 5 = not related.

TABLE 69 List of all adverse events (maximum grade) reported (as categorised by PIs) in the physiotherapy arm

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
Abdominal/ gastrointestinal	Vaginal discharge	10001	22 January 2013	1		5
	Abdominal pain	10032	08 March 2013	2		5
	Haemorrhoids	13060	22 January 2014	2		5
	Gastric bypass surgery	20267	29 March 2014	2	3	5
	Increased nausea	33507	UNK October 2014	2		4
Acute exacerbation of asthma	Asthma exacerbation	10001	24 September 2013	2		3
	Productive cough worsening (acute exacerbation of asthma)	18183	05 February 2014	1		3
	Acute exacerbation of asthma	25379	22 November 2014	2		3
	Exacerbation of asthma	25379	13 February 2015	2		3
	Exacerbation of asthma	31417	15 July 2014	2		3
	Asthma exacerbation	31432	12 October 2014	2		3
	COPD exacerbation	37537	03 August 2015	3		3
	Chest infection/asthma exacerbation	38576	28 September 2015	3		3
	Asthma exacerbation	38582	16 March 2015	3	3	3
	Asthma exacerbation	40600	24 March 2015	1		3
Chest pain and cardiovascular	Deep-vein thrombosis	10014	18 September 2013	3		5
	Chest pains with palpitations	12067	28 October 2013	2	3	5
	Pleuritic left-sided chest pain	19220	04 July 2014	1		4
	Chest pain	33507	20 October 2014	2		4
	Costochondritis	34460	15 July 2014	2		5
	Costal margin chest pain	43650	15 June 2015	1		5

continued

TABLE 69 List of all adverse events (maximum grade) reported (as categorised by PIs) in the physiotherapy arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
Increased asthma symptoms	Cough	10032	21 November 2013	1		3
	Wheeze plus shortness of breath	17110	15 March 2014	3		3
	Worsening of asthma	17123	11 December 2013	2		3
	Cough	17128	10 August 2014	1		3
	Wheeze	18175	17 September 2013	1		3
	One wheeze	18183	05 February 2014	1		3
	Wheeze	19220	06 January 2014	1		3
	Cough, dyspnoea and wheeze	23360	18 June 2014	1		3
	Cough	23362	27 October 2015	1		3
	Cough	24311	26 October 2014	1		3
	Worsening of asthma	25291	13 April 2014	1		3
	Increase in asthma symptoms	25305	01 October 2014	1		3
	Cough and wheeze	25379	13 March 2015	2		3
	Cough	26341	04 May 2014	1		3
	Cough	27338	23 February 2015	1		3
	Respiratory symptoms limiting exercise activities	31424	16 May 2015	1		3
	Cough	31486	03 September 2014	2		3
	Cough	32492	13 January 2015	2		3
	Increased cough, wheeze and shortness of breath	37550	13 April 2015	2		3
	Cough	38564	05 September 2015	1		3
Malignancy	Malignant lymphoma	10014	17 April 2013	3		5
Musculoskeletal	Shoulder pain	12040	01 July 2013	2		5
	Ankle and hip pain	13060	09 September 2013	3		4
	Back pain	13060	03 February 2014	3		5
	Joint aches (virus)	18183	12 September 2014	1		5
	Left-sided jaw pain	25325	12 September 2014	1		5
	Fractured right rib	31424	UNK January 2015	2		5
	Septic arthritis	38576	18 November 2014	3	3	5
	Sciatica	43635	19 March 2015	1		5
	Knee pain	43639	01 July 2015	1		5
	Shoulder pain	43643	28 July 2015	1		5

TABLE 69 List of all adverse events (maximum grade) reported (as categorised by PIs) in the physiotherapy arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
Neurological	Neuropathic pain	13060	27 June 2013	2		5
	Chronic inflammatory demyelinating polyneuropathy	21346	19 November 2014	2		5
	Tinnitus	36543	UNK November 2014	1		5
Psychological/ psychiatric	Anxiety	26321	UNK May 2014	1		3
	Stress	33519	UNK October 2014	2		4
Respiratory tract infection/cough	Sore throat	10032	01 September 2013	1		5
	Congestion with cold, cough and shortness of breath	17110	10 February 2014	2		5
	Sore throat (virus)	18183	12 September 2014	1		5
	Bronchitis	18219	UNK January 2014	1		5
	Green sputum	19220	06 January 2014	1		5
	Cough/cold	20250	24 December 2013	1		5
	Chest infection	21268	22 March 2014	1		4
	Viral cough	23284	29 December 2014	1		5
	Chest infection	23312	24 November 2014	1		5
	Viral illness causing wheeze, cough, fever and chest tightness	23343	28 December 2014	1		5
	Upper respiratory chest infection	23360	09 December 2014	1		5
	Cold	23362	26 January 2015	1		5
	Viral illness	25291	15 December 2014	1		5
	Cough and cold	25325	09 September 2014	1		5
	Chest infection	25330	17 July 2014	1		5
	Chest infection	25379	24 February 2015	2		5
	Cold	26321	28 January 2015	1		5
	Cold	26381	20 January 2015	1		5
	Chest infection	27338	11 December 2014	1		5
	Upper respiratory tract infection	28383	20 February 2015	1		5
	Upper respiratory tract infection	30399	27 December 2014	1		5
	Lower respiratory tract infection	31432	12 October 2014	2		4
	Cold virus (sore throat and cough)	37537	24 July 2015	2		5
	Sore throat	37550	13 April 2015	1		5

continued

TABLE 69 List of all adverse events (maximum grade) reported (as categorised by PIs) in the physiotherapy arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Chest infection	38593	25 September 2015	2		4
	Cough	39574	15 December 2014	2		5
Rhinitis/rhinosinusitis	Chronic rhinitis	18183	12 September 2014	1		5
	Earache/congested sinuses	25325	20 October 2014	1		5
	Nasal congestion	28383		2		5
	Left ear infection	31419	UNK June 2014	2		4
	Runny nose	32492	13 January 2015	2		5
Miscellaneous	Urinary tract infection	10014	29 May 2013	2		5
	Itch	12040	19 February 2014	1		4
	Otitis externa	13047	21 October 2013	1		5
	Calf pain	13060	18 July 2013	3		5
	Blepharitis	13072	13 March 2014	1		5
	Pyrexia (virus)	18183	12 September 2014	1		5
	Virus affecting ears, throat and stomach	28387	13 March 2015	1		5
	Oral thrush	31474	03 February 2015	1		5
	Acute tonsillitis	34514	20 June 2015	2		5
	Hoarseness	38564	14 November 2014	1		5

UNK, unknown.
a Grade: 1 = mild, 2 = moderate, 3 = severe, 4 = life-threatening, 5 = death related to adverse event.
b Why was the event serious?: 1 = resulted in death, 2 = life-threatening, 3 = required hospitalisation or prolongation of existing hospitalisation, 4 = resulted in persistent or significant disability/incapacity, 5 = congenital anomaly/birth defect.
c Investigator's opinion – causal relationship to adverse event: 1 = definitely, 2 = probably, 3 = possibly, 4 = unlikely, 5 = not related.

TABLE 70 List of all adverse events (maximum grade) reported (as categorised by PIs) in the usual-care arm

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
Abdominal/ gastrointestinal	Rectal bleeding	10005	01 July 2013	2		5
	Altered bowel habit – complains of adhesions	10013	14 December 2013	2		5
	Bacterial vaginosis	10021	19 June 2013	2		5
	Laparoscopic vaginal hysterectomy	12068	17 March 2014	3	3	5
	Gastritis	12127	31 October 2013	2	3	5
	Abdominal pain	12195	01 September 2014	3	3	5
	Epigastric pain plus dysfunctional breathing	13073	23 September 2013	2		5

TABLE 70 List of all adverse events (maximum grade) reported (as categorised by PIs) in the usual-care arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Colitis	15203	31 July 2014	3	3	5
	Vomiting (flu)	16187	UNK December 2013	1		5
	Epigastric pain episode linked to ongoing acid reflux	27349	07 October 2014	1		5
	Lower abdominal pain	31434	13 June 2014	2		4
	Gastritis	32416	UNK September 2014	2		5
	Abdominal pain	34459	12 May 2015	1		5
	Lower abdominal pain with loose stools	34500	01 December 2014	2		4
	Per vaginal bleed post large loop excision of the transformation zone of the cervix	37547	15 July 2015	2	3	5
	Umbilical hernia repair	38572	17 February 2015	3	3	5
Acute exacerbation of asthma	Asthma exacerbation	10030	03 January 2014	3		3
	Exacerbation of asthma/ COPD	12057	08 January 2014	2		3
	Asthma exacerbation	12068	25 August 2013	2		3
	Exacerbation of asthma	12137	20 March 2014	2		3
	Asthma exacerbation	17125	20 January 2014	2		3
	COPD	17173	10 September 2013	2		3
	Asthma exacerbation	18182	UNK May 2014	2		3
	Exacerbation of asthma	23283	17 March 2014	1		3
	Asthma exacerbation	23342	01 August 2014	1		3
	One exacerbation of asthma	26350	08 April 2014	1		3
	Exacerbation of asthma	31425	UNK November 2014	1		3
	One exacerbation of asthma	31429	12 February 2015	1		3
	Acute exacerbation of asthma	31434	13 November 2014	2		3
	Asthma exacerbation	31436	24 May 2014	1		3
	Asthma exacerbation	31503	30 October 2014	2		3
	Acute exacerbation of asthma	34499	23 February 2015	2		3
	Acute exacerbation of asthma	34500	21 January 2015	2		3
	Asthma exacerbation	34515	06 May 2015	2		3
	Asthma exacerbation	36555	09 February 2015	3		3

continued

TABLE 70 List of all adverse events (maximum grade) reported (as categorised by PIs) in the usual-care arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Exacerbation of asthma	38572	19 October 2014	3		3
	Infective exacerbation of asthma	39575	09 January 2015	3	3	3
	Exacerbation of asthma	42616	13 July 2015	1		3
	Exacerbation of asthma	43641	11 September 2015	1		3
Chest pain and cardiovascular	Palpitations	12043	15 August 2013	2		3
	Chest pain	12091	28 December 2013	2	3	5
	Chest pain? – hiatus hernia	12195	26 May 2014	2	3	5
	High blood pressure	13066	30 May 2014	3		4
	Chest pain	13073	04 October 2013	3		5
	Collapsed and died – post mortem report found pulmonary oedema with a background of dilated cardiomyopathy and thyroid disease	14095	26 April 2014	1	3	5
	Chest pain	18184	16 October 2013	1		5
	Rib pain	20260	24 February 2014	1		5
	Chest pain	28390	UNK November 2014	2		5
	Palpitations	31434	24 March 2015	3	3	4
	Chest pain – acute coronary syndrome	32449	10 September 2014	3	3	5
	Exertional chest pain (while hovering)	33510	02 September 2014	2		4
	Chest pain	34477	24 December 2014	2	3	5
	Pulmonary embolism	38570	22 November 2014	3	3	5
	Atrial fibrillation	38572	02 August 2015	3		5
	Palpitations	40608	09 November 2015	1		5
Increased asthma symptoms	Wheeze tachycardia	11017	02 May 2013	3	3	3
	Worsening of asthma	12137	17 January 2014	2		3
	Wheeze	16147	UNK December 2013	2		3
	Cough	17125	01 December 2013	2		3
	Cough	17173	04 April 2014	1		3
	Cough	18170	05 May 2014	1		3
	Shortness of breath	18184	28 February 2014	2		3
	Cough	18211	02 December 2013	1		3
	Wheeze	19228	06 October 2014	1		3
	Cough	21282	21 December 2014	1		3
	Cough	23342	25 April 2014	1		3

TABLE 70 List of all adverse events (maximum grade) reported (as categorised by PIs) in the usual-care arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Cough and wheeze	24357	16 March 2015	1		3
	Shortness of breath	25293	02 June 2014	1		3
	Ongoing asthma symptoms	25294	14 April 2014	1		3
	Slight breathlessness	25324	17 September 2014	1		3
	Cough	25412	31 August 2014	1		3
	Cough and wheeze	27333	24 September 2014	1		3
	Asthma symptoms	30398	UNK September 2014	1		3
	Tight chest	31422	16 May 2014	2		3
	Shortness of breath	31470	26 April 2015	2		3
	Poor asthma control	31503	18 February 2015	2		3
	Slight wheeze	32400	08 January 2015	2		3
	Cough	32403	UNK November 2014	2		3
	Increasing shortness of breath	33504	12 July 2014	2		3
	Cough	34440	11 November 2014	1		3
	Breathlessness	34459	UNK December 2014	2		3
	Cough and wheeze	34515	29 June 2015	2		3
	Asthma worsening	37527	UNK January 2015	1		3
	Cough and wheeze	37547	18 May 2015	2		3
	Wheeze and shortness of breath	38567	14 December 2014	2		3
	Shortness of breath on exertion	38604	28 February 2015	2		3
	Cough	42615	29 December 2014	1		5
Musculoskeletal	Degenerative change in lumbosacral region	10005	21 May 2013	2		5
	Back pain	10024	30 September 2013	2		5
	Arthralgia of hands/ shoulders	12100	24 March 2014	2		5
	Shoulder pain	13046	18 March 2014	3		5
	Cervicalgia	17099	09 June 2014	2		5
	Neck pain	17173	20 May 2014	1		5
	Joint ache	19228	06 October 2014	1		5
	Right knee replacement surgery	23280	01 December 2014	2	3	5
	Neck pain	26317	13 July 2014	1		5
	Low back pain	31406	UNK July 2014	2		4

continued

TABLE 70 List of all adverse events (maximum grade) reported (as categorised by PIs) in the usual-care arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Right shoulder rotator cuff tear	31421	16 November 2014	3		5
	Gout	31422	27 March 2015	2		4
	Prolapsed intervertebral lumbar disc (worsening of)	31425	31 October 2014	2		4
	Right shoulder rotator cuff sprain	31429	02 September 2014	2		4
	Worsening of frozen shoulder (right)	31437	UNK April 2015	2		4
	Rotator cuff syndrome	31445	UNK January 2014	1		4
	Back pain	33513	23 February 2015	1		4
	Cervicalgia	34500	13 May 2015	2		4
	Left-sided muscle tightness in neck	35541	17 May 2015	1		4
	Cervicalgia	35544	UNK January 2015	3		5
	Tennis elbow	43630	17 November 2015	1		5
	Rotator cuff syndrome	43641	06 May 2015	2		5
Neurological	Tremor	10021	12 November 2013	1		5
	Neuralgic pain	13046	15 November 2013	2		5
	Headache	19228	06 October 2014	1		5
	Dizziness	31425	UNK July 2014	2		4
	Nausea	31434	24 March 2015	2	3	4
	Cerebral venous thrombosis	31501	04 July 2014	3	3	5
	Headache	33504	12 July 2014	2		4
	Light-headed symptoms	33513	03 June 2015	1		4
	Giant cell arteritis	38570	24 October 2014	3	3	5
	Post FeNO test breathlessness, light-headedness and clammy	38572	30 September 2015	2		5
	Migraine	43649	05 March 2015	1		5
Psychological/ psychiatric	Mood swings	10021	08 May 2013	2		3
	Anxiety (worsening)	12043	24 September 2013	3		3
	Lethargy	13046	08 October 2013	2		5
	Anxiety with depression	13073	13 June 2014	3		3
	Shortness of breath (panic attack)	16151	15 April 2014	1		3
	Anxiety	17099	06 August 2013	2		3
	Anxiety	17125	27 June 2014	2		3
	Depression	21282	UNK November 2014	1		3

TABLE 70 List of all adverse events (maximum grade) reported (as categorised by PIs) in the usual-care arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Depression	23344	UNK October 2014	1		3
	Depression	25378	15 October 2014	1		3
	Low mood	31406	UNK December 2014	2		3
	Depression	31429	02 April 2015	2		3
	Recurrence of depressive episode	31437	UNK October 2014	2		3
	Low mood	31484	28 January 2015	2		3
	Anxiety	32416	UNK September 2014	2		3
	Anxiety attack	33504	30 March 2015	2	3	3
Respiratory tract infection/cough	Acute lower respiratory tract infection	12057	24 May 2014	2	3	4
	Lower respiratory tract infection	12062	11 February 2014	2		5
	Chest infection	12068	26 March 2014	2		5
	Upper respiratory tract infection	12075	24 December 2013	2		5
	Chesty cough	12082	10 January 2014	1		5
	Cough ongoing	12137	31 March 2014	2		5
	Sore throat	16139	16 August 2014	1		5
	Productive cough	16147	UNK December 2013	2		5
	Shortness of breath (flu)	16187	UNK December 2013	1		5
	Pneumonia	17173	23 July 2014	3	3	5
	Cough (post viral)	18182	UNK March 2014	1		5
	Stridor	18184	02 March 2014	2	3	5
	Dry cough	18209	15 August 2014	1		5
	Productive cough	18216	19 March 2014	1		5
	Cough with green phlegm	19240	UNK December 2013	1		5
	Chest infection	20246	11 November 2013	1		5
	Chest infection	20260	10 November 2013	1		5
	Chesty cough	20265	22 August 2014	1		5
	Chest infection	20277	UNK May 2014	1		5
	Cold	21270	24 November 2014	1		5
	Lower respiratory tract infection	21282	04 October 2014	1		5
	Bronchitis	22276	UNK December 2013	1		4
	One episode of coughing	23280	15 October 2014	1		5
	Viral infection (green sputum, cough)	23283	08 December 2014	1		5

continued

TABLE 70 List of all adverse events (maximum grade) reported (as categorised by PIs) in the usual-care arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Chest infection	23287	01 December 2014	1		5
	Flu-like virus	23288	31 December 2014	1		5
	Chest infection	23342	04 April 2014	1		5
	Chest infection	24309	18 December 2014	1		5
	Chest infection	24357	24 January 2015	1		5
	Respiratory heart infection	25294	01 April 2014	1		5
	Sore throat	25324	29 December 2014	1		5
	Pharyngitis	25329	01 May 2014	1		5
	Cold	25331	15 December 2014	1		5
	Cold	25412	11 April 2015	1		5
	Cough? viral laryngitis	26317	18 August 2014	1		5
	Cough with green sputum	26335	25 November 2014	1		5
	Upper respiratory tract infection	26339	18 October 2014	1		5
	Upper respiratory tract infection	26350	30 January 2015	1		5
	Cough and cold	26371	17 February 2015	1		5
	Chesty cough	27349	28 May 2014	1		5
	Upper respiratory tract infection	28388	26 February 2015	1		5
	Chest infection	29413	01 April 2015	1		5
	Chest infection	29462	15 April 2015	1		5
	Influenza A	30395	26 December 2014	3	3	5
	Lower respiratory tract infection	30398	20 December 2014	1		5
	Sore throat	31422	02 March 2015	1		4
	Haemoptysis	31434	24 March 2015	2	3	4
	Productive cough	31436	24 May 2014	2		4
	Chest infection	31482	30 December 2014	2		4
	Chesty cough	31503	03 February 2015	2		4
	Sore throat	32400	08 January 2015	2		5
	Night cough	32488	01 March 2015	2		4
	Chesty cough	33504	UNK November 2014	1		4
	Cold virus	34439	15 October 2014	1		5
	Chest infection	34458	UNK April 2015	1		5
	Chest infection	34496	25 February 2015	2		4
	Chest infection	34499	23 November 2014	2		4
	Coryzal	35544	25 June 2015	3		5

TABLE 70 List of all adverse events (maximum grade) reported (as categorised by PIs) in the usual-care arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
	Pharyngitis	36533	25 March 2015	1		5
	Chest rattle	36552	10 August 2015	1		4
	Cough, wheeze, shortness of breath, crackles and phlegm	36555	27 October 2014	3		4
	Upper respiratory tract infection	37547	25 February 2015	2		5
	Pseudomonas aeruginosa infection	38563	17 May 2015	3		4
	Acute laryngitis	38567	22 June 2015	2		5
	Lower respiratory tract infection	38570	02 December 2014	3	3	5
	Sore throat – fungal mouth infection	38581	27 January 2015	2		5
	Cold virus	38583	11 October 2015	1		5
	Chest infection	38590	24 January 2015	1		5
	Bronchiectasis – infective exacerbation	38591	07 September 2015	1		5
	Cold virus	38636	28 November 2015	1		5
	Cough	39611	18 April 2015	1		5
	Cough	42620	29 April 2015	1		5
Rhinitis/rhinosinusitis	Acute sinusitis	10036	30 January 2014	2		5
	Acute sinusitis	12137	27 May 2014	1		5
	Congestion	18209	15 August 2014	1		5
	Nasal congestion	19228	06 October 2014	1		5
	Acute sinusitis	20260	15 September 2014	1		5
	Allergic rhinitis	20265	05 May 2014	1		5
	Sinusitis	23342	16 January 2015	1		5
	Sinusitis	25293	06 August 2014	1		5
	Allergic rhinitis	27349	12 June 2014	1		5
	Eustachian tube dysfunction	31429	11 March 2015	1		4
	Acute sinusitis	33510	UNK December 2014	2		4
	Sinus pain	34440	UNK March 2015	1		5
	Sinusitis	37547	01 March 2015	2		5
	Sinusitis	38563	17 August 15	2		4
	Rhinitis	38606	05 July 2015	2		5
	Acute sinusitis	43641	09 December 2015	1		5

continued

TABLE 70 List of all adverse events (maximum grade) reported (as categorised by PIs) in the usual-care arm (*continued*)

Category of main symptom	Nature of adverse event	Patient ID	Date of onset	Severity of adverse event[a]	Serious[b]	Causality[c]
Miscellaneous	Anaemia	10021	18 February 2013	2		5
	Open wound on scalp	10030	28 June 2013	1		5
	Problems with crumbling teeth	12042	21 August 2013	2	3	5
	Balanitis	12043	21 March 2014	1		5
	Contact dermatitis	12068	12 November 2013	1		5
	Excision of thyroglossal cyst	13046	01 October 2013	2		5
	Dysfunctional breathing	13073	03 September 2013	2		5
	Pyrexia	18184	28 February 2014	2		5
	Pleural effusion	20238	11 April 2014	1	3	5
	Flu symptoms	23319	UNK February 2014	1		5
	Urinary tract infection	25294	27 July 2014	2	3	5
	Cough? gastric reflux? post-nasal drip	25375	UNK August 2014	1		5
	Neck swelling	26350	06 January 2015	1		5
	Oral thrush	29462	24 September 2014	1		5
	Fever	31434	24 March 2015	2	3	4
	Seborrheic dermatitis	31437	UNK October 2014	2		5
	Oral thrush	31450	18 December 2014	1		4
	Oral thrush	31503	11 March 2015	2		4
	Tonsillitis	38587	10 September 2015	3	3	5

UNK, unknown.

a Grade: 1 = mild, 2 = moderate, 3 = severe, 4 = life-threatening, 5 = death related to adverse event.

b Why was the event serious?: 1 = resulted in death, 2 = life-threatening, 3 = required hospitalisation or prolongation of existing hospitalisation, 4 = resulted in persistent or significant disability/incapacity, 5 = congenital anomaly/birth defect.

c Investigator's opinion – causal relationship to adverse event: 1 = definitely, 2 = probably, 3 = possibly, 4 = unlikely, 5 = not related.

Appendix 12 Unit costs of the interventions and primary care and other service use

TABLE 71 Unit costs of the interventions and primary care and other service use (2014/15 prices)

Service	Unit cost (£)	Source
GP consultation	45.00	PSSRU[73]
Out-of-hours clinic	135.00	PSSRU[73]
Walk-in clinic	135.00	PSSRU[73]
Outpatient	135.00	PSSRU[73]
A&E visit	177.00	PSSRU[73]
Inpatient admission	2581.00	*NHS Reference Costs 2014 to 2015*[74]
Intervention: face-to-face physiotherapy	83.45	Trial estimate
Intervention: DVD	2.85	Trial estimate

Appendix 13 Correlation coefficients (Pearson's *r*) between expectancy, experience and practical barriers associated with amount of practice (at 3 months) and continued engagement (at 6 and 12 months)

TABLE 72 Correlation coefficients (Pearson's *r*) between expectancy, experience and practical barriers associated with amount of practice (at 3 months) and continued engagement (at 6 and 12 months)

Expectancy, experience and practical barriers	Amount of practice at 3 months		Continued engagement at			
			6 months		12 months	
	DVD	Physiotherapy	DVD	Physiotherapy	DVD	Physiotherapy
Expectancy						
Beliefs about asthma						
Perceived causes						
Cause 1 – allergy	0.14	0.20*	–0.00	–0.02	0.03	0.01
Cause 2 – health issues	–0.07	–0.05	–0.09	–0.03	–0.21**	0.08
Cause 3 – smoking	0.20*	0.05	0.05	0.17	0.10	0.27**
Perceived chronicity						
All the time	0.06	0.11	0.11	0.01	0.03	0.04
Most of the time	–0.25**	–0.02	–0.11	0.06	–0.11	0.01
Some of the time	0.12	–0.07	0.00	–0.06	0.07	–0.13
Only when symptoms are present	0.02	–0.05	–0.02	–0.00	–0.00	0.09
First impressions of treatment						
Expectancy	0.21**	0.02	0.23**	0.14	0.16	–0.05
Self-efficacy	0.33***	–0.04	0.38***	0.20	0.35***	–0.05
Perceived need for support (baseline)	–0.01	–0.03	–0.03	0.06	–0.10	–0.06
TPB: perceived behavioural control	0.16*	–0.07	0.27***	0.06	0.15	0.03
TPB: intentions	0.14	–0.01	0.17*	0.13	0.19*	0.09
Treatment experience						
Enjoyment of treatment						
Stomach breathing	0.39***	0.30**	0.37***	0.29**	0.34***	0.24*
Nose breathing	0.39***	0.30**	0.36***	0.23*	0.39***	0.19
Slow breathing	0.36***	0.11	0.32***	0.18	0.32***	0.24*
Controlled breath holding	0.26***	0.05	0.24**	0.25*	0.24**	0.27*
Relaxation training	0.39***	0.10	0.32***	0.35***	0.25**	0.36***

continued

TABLE 72 Correlation coefficients (Pearson's *r*) between expectancy, experience and practical barriers associated with amount of practice (at 3 months) and continued engagement (at 6 and 12 months) (*continued*)

Expectancy, experience and practical barriers	Amount of practice at 3 months		Continued engagement at			
			6 months		12 months	
	DVD	Physiotherapy	DVD	Physiotherapy	DVD	Physiotherapy
Appointments with physiotherapist (physiotherapy group only)		0.19		0.01		0.04
Perceived need for support (3 months)	–0.16*	0.26*	–0.11	0.10	–0.14	0.32**
Perceptions of physiotherapist (physiotherapy group only)		0.21*		0.09		0.09
Practical barriers						
PETS						
Problems due to symptoms	–0.10	–0.09	–0.18*	0.15	–0.03	0.07
Problems due to uncertainty	–0.32***	–0.15	–0.29***	0.10	–0.07	0.07
Problems due to doubts	–0.46***	–0.20*	–0.45***	–0.15	–0.30***	–0.05
Practical problems	–0.38***	–0.30**	–0.33***	–0.15	–0.32***	–0.12
Problems due to lack of support	–0.25***	–0.25**	–0.24**	–0.16	–0.18	–0.01

*$p \leq 0.05$, **$p < 0.01$, ***$p < 0.001$.
TPB, theory of planned behaviour.

Appendix 14 Multiple regression results for expectancy, experience and practical barrier variables associated with amount of practice (at 3 months)

TABLE 73 Multiple regression results for expectancy, experience and practical barrier variables associated with amount of practice (at 3 months)

	B	SE (B)	β	95% CI
Perceived causes				
Cause 1 – allergy	20.15	10.65	0.22	–1.11 to 41.41
Cause 3 – smoking	8.11	11.08	0.08	–14.01 to 30.24
Perceived chronicity				
Most of the time	6.52	13.57	0.05	–20.57 to 33.61
First impressions of treatment				
Expectancy	–1.60	2.11	–0.09	–5.80 to 2.61
Self-efficacy	0.13	4.54	0.00	–8.94 to 9.21
TPB: perceived behavioural control	–2.32	2.29	–0.11	–6.89 to 2.24
Enjoyment of treatment				
Stomach breathing	1.91	4.91	0.07	–7.89 to 11.71
Nose breathing	6.63	3.95	0.25	–1.25 to 14.51
Slow breathing	1.61	3.68	0.07	–5.74 to 8.96
Controlled breath holding	–3.82	3.58	–0.16	–10.97 to 3.33
Relaxation training	–2.25	2.46	–0.12	–7.15 to 2.65
Perceived need for support (3 months)	5.29	9.10	0.07	–12.89 to 23.46
Perceptions of physiotherapist (physiotherapy group only)	9.02	14.52	0.08	–19.97 to 38.00
PETS				
Problems due to uncertainty	–11.37	15.69	–0.08	–42.69 to 19.96
Problems due to doubts	–2.52	14.40	–0.02	–31.27 to 26.23
Practical problems	–28.44	14.05	–0.24*	–56.49 to –0.39
Problems due to lack of support	–29.86	14.95	–0.23*	–59.72 to –0.00

*$p \leq 0.05$.
SE, standard error; TPB, theory of planned behaviour.
$R^2 = 0.33$, $F_{17,66} = 1.92$* ($n = 84$).

Appendix 15 Multiple regression results for expectancy, experience and practical barrier variables associated with continued engagement (at 6 months)

TABLE 74 Multiple regression results for expectancy, experience and practical barrier variables associated with continued engagement (at 6 months)

	B	SE (B)	β	95% CI
First impressions of treatment				
Expectancy	0.10	0.13	0.06	–0.15 to 0.35
Self-efficacy	0.17	0.30	0.05	–0.43 to 0.76
TPB: perceived behavioural control	–0.11	0.17	–0.06	–0.45 to 0.23
TPB: intentions	0.73	0.78	0.08	–0.81 to 2.28
Enjoyment of treatment				
Stomach breathing	0.32	0.24	0.13	–0.16 to 0.79
Nose breathing	0.31	0.23	0.13	–0.15 to 0.76
Slow breathing	–0.19	0.28	–0.08	–0.73 to 0.36
Controlled breath holding	–0.00	0.22	–0.00	–0.44 to 0.43
Relaxation training	0.41	0.19	0.18*	0.04 to 0.79
PETS				
Problems due to symptoms	1.75	0.88	0.16*	0.00 to 3.49
Problems due to uncertainty	0.34	0.90	0.03	–1.43 to 2.12
Problems due to doubts	–2.20	0.86	–0.22**	–3.89 to –0.50
Practical problems	–1.28	0.93	–0.10	–3.11 to 0.54
Problems due to lack of support	–0.88	0.82	–0.08	–2.51 to 0.74

*$p \leq 0.05$, **$p < 0.01$, ***$p < 0.001$.
SE, standard error; TPB, theory of planned behaviour.
$R^2 = 0.24$, $F_{14,174} = 3.97$*** ($n = 189$).

Appendix 16 Multiple regression results for expectancy, experience and practical barrier variables associated with continued engagement (at 12 months)

TABLE 75 Multiple regression results for expectancy, experience and practical barrier variables associated with continued engagement (at 12 months)

	B	SE (B)	β	95% CI
Perceived causes				
Cause 2 – health issues	–0.65	0.66	–0.07	–1.95 to 0.65
Cause 3 – smoking	1.19	0.70	0.12	–0.19 to 2.57
First impressions of treatment				
Self-efficacy	0.17	0.27	0.05	–0.36 to 0.70
TPB: intentions	–0.09	0.68	–0.01	–1.44 to 1.26
Enjoyment of treatment				
Stomach breathing	0.16	0.26	0.07	–0.35 to 0.67
Nose breathing	0.36	0.22	0.17	–0.08 to 0.80
Slow breathing	–0.02	0.27	–0.01	–0.55 to 0.51
Controlled breath holding	0.01	0.21	0.01	–0.40 to 0.42
Relaxation training	0.29	0.19	0.14	–0.08 to 0.67
Perceived need for support (3 months)	–0.17	0.23	–0.06	–0.62 to 0.28
PETS				
Problems due to doubts	–0.28	0.74	–0.03	–1.74 to 1.19
Practical problems	–1.27	0.87	–0.11	–2.99 to 0.45

$***p < 0.001$.
SE, standard error; TPB, theory of planned behaviour.
$R = 0.17$, $F_{12,173} = 3.05***$ ($n = 186$).

Appendix 17 Correlation coefficients (Pearson's *r*) between the components of the theory of planned behaviour

TABLE 76 Correlation coefficients (Pearson's *r*) between the components of the theory of planned behaviour

	1	2	3	4	5	6	7	8	9
1. Attitude ($\alpha = 94$)									
2. Subjective norms ($\alpha = 0.98$)	0.71***								
3. Perceived behavioural control ($\alpha = 0.89$)	0.26***	0.20***							
4. Intentions ($\alpha = 0.96$)	0.24***	0.25***	0.58***						
5. Beliefs (attitude related) ($\alpha = 0.87$)	0.44***	0.29***	0.55***	0.36***					
6. Beliefs (control related –1) – time-consuming	0.21***	0.17***	0.23***	0.16**	0.05				
7. Beliefs (control related –2) – fit daily routine	0.26***	0.25***	0.35***	0.27***	0.15**	0.53***			
8. Amount of practice	0.13*	0.12	0.14*	0.12	0.15**	0.27***	0.21***		
9. Continued engagement (6 months)	0.13*	0.05	0.24***	0.17**	0.24***	0.32***	0.32***	0.51***	
10. Continued engagement (12 months)	0.05	0.03	0.15*	0.17**	0.18**	0.22***	0.19**	0.55***	0.76***

*$p \leq 0.05$, **$p < 0.01$, ***$p < 0.001$.

Appendix 18 Hierarchical logistic regression results for the role of attitude, subjective norms and perceived behavioural control in the prediction of intentions

TABLE 77 Hierarchical logistic regression results for the role of attitude, subjective norms and perceived behavioural control in the prediction of intentions

	B	SE (B)	Wald	Odds ratio [exp(B)]	95% CI
Attitude	–0.03	0.06	0.26	0.97	0.86 to 1.10
Subjective norms	0.09	0.05	3.20	1.10	0.99 to 1.22
Perceived behavioural control	0.79	0.11	54.95***	2.21	1.79 to 2.72
Beliefs (attitude related)	0.04	0.05	0.93	1.04	0.96 to 1.14
Beliefs (control related –1) – time-consuming	–0.05	0.09	0.30	0.95	0.79 to 1.14
Beliefs (control related –2) – fit daily routine	0.01	0.10	0.01	1.01	0.83 to 1.23

***$p < 0.001$.
SE, standard error.
Model χ^2 [degrees of freedom (df) = 6, $n = 336$] = 154.23, $p < 0.001$; Nagelkerke $R^2 = 0.49$; Hosmer–Lemeshow χ^2 (df = 8) = 49.92, $p < 0.001$).

Appendix 19 Hierarchical linear regression results for the role of intention and perceived behavioural control in the prediction of continued engagement (at 6 months)

TABLE 78 Hierarchical linear regression results for the role of intention and perceived behavioural control in the prediction of continued engagement (at 6 months)

	B	SE (B)	β	95% CI
Step 1				
Intention	1.72	0.63	0.17**	0.48 to 2.95
Step 2				
Intention	0.53	0.77	0.05	–0.99 to 2.04
Perceived behavioural control	0.40	0.15	0.20**	0.10 to 0.70

$^{**}p < 0.01$, $^{***}p < 0.001$.
SE, standard error.
$R^2 = 0.03$, $F_{2,242} = 7.31^{***}$ ($n = 245$).

Appendix 20 Hierarchical multiple regression results for the role of intention and perceived behavioural control in the prediction of continued engagement (at 12 months)

TABLE 79 Hierarchical multiple regression results for the role of intention and perceived behavioural control in the prediction of continued engagement (at 12 months)

	B	SE (B)	β	95% CI
Step 1				
Intention	1.55	0.59	0.17**	0.40 to 2.71
Step 2				
Intention	1.20	0.72	0.13	–0.22 to 2.61
Perceived behavioural control	0.12	0.14	0.07	–0.16 to 0.40

*$p \leq 0.05$, **$p < 0.01$.
SE, standard error.
$R^2 = 0.03$, $F_{2,238} = 3.87$* ($n = 241$).

Appendix 21 Hierarchical multiple regression results for the role of intention and perceived behavioural control in the prediction of amount of practice (at 3 months)

TABLE 80 Hierarchical multiple regression results for the role of intention and perceived behavioural control in the prediction of amount of practice (at 3 months)

	B	SE (B)	β	95% CI
Step 1				
Intention	10.71	5.80	0.11	–0.72 to 22.14
Step 2				
Intention	4.78	6.87	0.05	–8.75 to 18.32
Perceived behavioural control	2.18	1.36	0.12	–0.50 to 4.86

*$p \leq 0.05$.
SE, standard error.
$R^2 = 0.01$, $F_{2,257} = 2.99$* ($n = 260$).

Appendix 22 Principal axis factoring (pattern matrix) and internal consistency of the Problematic Experiences of Therapy Scale items

TABLE 81 Principal axis factoring (pattern matrix) and internal consistency of the PETS items

Items	I	II	III	IV	V
I. Problems due to symptoms ($\alpha = 0.76$)					
1. I had to skip the breathing retraining because it made my symptoms worse	0.827				
2. I was prevented from carrying out the breathing retraining by severe symptoms	0.919				
3. I could not carry out the breathing retraining because it caused more symptoms					
II. Problems due to uncertainty ($\alpha = 0.89$)					
4. I could not carry out the breathing retraining because I was unsure how to do it properly		–0.880			
5. I was unable to carry out the breathing retraining because it was difficult to know what to do					
6. I did not carry out the breathing retraining because I was worried that I was doing it wrong		–0.755			
III. Problems due to doubts ($\alpha = 0.90$)					
7. I skipped the breathing retraining because I was not sure if it was helping			–0.881		
8. I skipped the breathing retraining because it did not seem relevant to my symptoms and problems			–0.880		
9. I did not carry out the breathing retraining because I was not convinced it was right for me			–0.915		
IV. Practical problems ($\alpha = 0.89$)					
10. Lack of time prevented me from carrying out the breathing retraining				0.944	
11. It was not possible to find suitable opportunities to carry out the breathing retraining				0.891	
12. I was too busy to carry out the breathing retraining				0.910	
13. I was too tired to carry out the breathing retraining				0.631	
14. I found it difficult to remember to carry out the breathing retraining				0.646	
V. Problems due to lack of support ($\alpha = 0.85$)					
15. I did not carry out the breathing retraining because I did not receive enough support from my family and friends					0.792
16. Lack of support from a health professional prevented me from carrying out the breathing retraining					0.822
17. I did not carry out the breathing retraining because I did not have anyone to support me					0.931
Item variance accounted for by factor (%)	6.64	4.77	15.25	15.25	44.49

Appendix 23 Component Pearson's correlation matrices of the Problematic Experiences of Therapy Scale subscales

TABLE 82 Component Pearson's correlation matrices of the PETS subscales

Subscale	I	II	III	IV	V
I. Problems due to symptoms					
II. Problems due to uncertainty	–0.337				
III. Problems due to doubts	–0.326	0.489			
IV. Practical problems	0.166	–0.299	–0.292		
V. Problems due to lack of support	0.371	–0.501	–0.448	0.491	

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